STIC Search Report
Biotech-Chem Library

STIC Database Tracking Number: 156107

TO: Ralph J Gitomer
Location: REM-3D65&3E71
Art Unit: 1651
Thursday, June 23, 2005

Case Serial Number: 10/679485

From: Noble Jarrell
Location: Biotech-Chem Library
Rem 1B71
Phone: 272-2556

Noble.jarrell@uspto.gov

Search Notes

```
=> b reg
FILE 'REGISTRY' ENTERED AT 07:52:32 ON 23 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
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Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES:    22 JUN 2005  HIGHEST RN 852803-45-3
DICTIONARY FILE UPDATES:  22 JUN 2005  HIGHEST RN 852803-45-3

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.

*********************************************************************
*                                                                   *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added,   *
* effective March 20, 2005.  A new display format, IDERL, is now    *
* available and contains the CA role and document type information. *
*                                                                   *
*********************************************************************

Crossover limits have been increased.  See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more
information enter HELP PROP at an arrow prompt in the file or refer
to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=> d ide l5 tot

L5   ANSWER 1 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   291762-73-7  REGISTRY
ED   Entered STN:  29 Sep 2000
CN   4-Octadecene-1,3-diol, 2-amino-, labeled with tritium, (2S,3R,4E)-
     (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C18 H37 N O2
SR   CA
LC   STN Files:   CA, CAPLUS
IL   XH-3

Absolute stereochemistry.
Double bond geometry as shown.
```
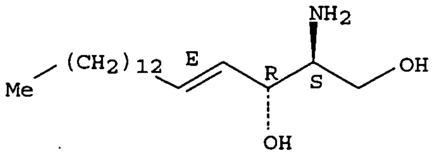
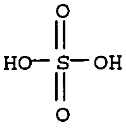
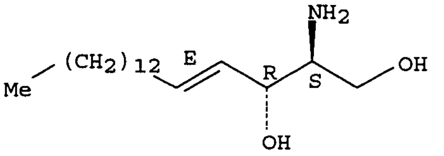



```
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 2 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   207516-16-3  REGISTRY
ED   Entered STN:  24 Jun 1998
CN   4-Octadecene-1,3-diol, 2-amino-, (2S,3R,4E)-, sulfate (1:1) (salt)
```

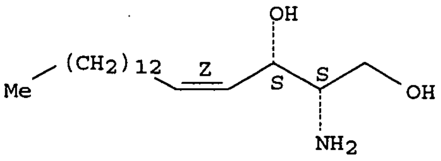
```
     (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C18 H37 N O2 . H2 O4 S
SR   CA
LC   STN Files:   CA, CAPLUS

     CM   1

     CRN  7664-93-9
     CMF  H2 O4 S
```



```
     CM   2

     CRN  123-78-4
     CMF  C18 H37 N O2

Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
```



```
               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 3 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   157240-87-4  REGISTRY
ED   Entered STN:  25 Aug 1994
CN   4-Octadecene-1,3-diol, 2-amino-, [S-[R*,R*-(Z)]]- (9CI)  (CA
     INDEX NAME)
FS   STEREOSEARCH
MF   C18 H37 N O2
SR   CA
LC   STN Files:   CA, CAPLUS

Absolute stereochemistry.
Double bond geometry as shown.
```



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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)
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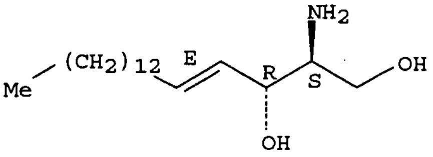
L5   ANSWER 4 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   153736-68-6  REGISTRY
ED   Entered STN:  18 Mar 1994
CN   4-Octadecene-1,3-diol, 2-amino-, [R-[R*,S*-(E)]]-, mixt. with
     [2R-[2R*(4R*,8R*)]]-3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-
     trimethyltridecyl)-2H-1-benzopyran-6-ol (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2H-1-Benzopyran-6-ol, 3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-
     trimethyltridecyl)-, [2R-[2R*(4R*,8R*)]]-, mixt. contg. (9CI)
FS   STEREOSEARCH
MF   C29 H50 O2 . C18 H37 N O2
CI   MXS
SR   CA
LC   STN Files:   CA, CAPLUS

     CM   1

     CRN  123-78-4
     CMF  C18 H37 N O2

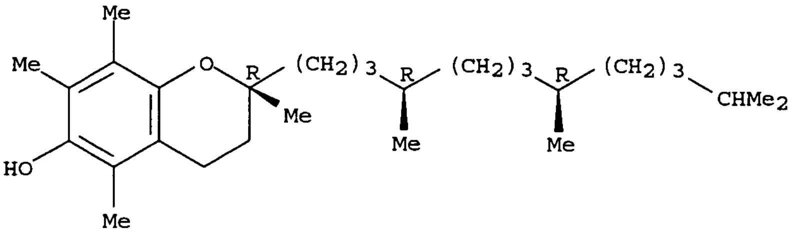
Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
```



```
     CM   2

     CRN  59-02-9
     CMF  C29 H50 O2

Absolute stereochemistry.
```



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               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 5 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   153736-67-5  REGISTRY
ED   Entered STN:  18 Mar 1994
CN   4-Octadecene-1,3-diol, 2-amino-, [R-[R*,S*-(E)]]-, mixt. with
     [2R-[2R*(4R*,8R*)]]-3,4-dihydro-2,8-dimethyl-2-(4,8,12-trimethyltridecyl)-
     2H-1-benzopyran-6-ol (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   2H-1-Benzopyran-6-ol, 3,4-dihydro-2,8-dimethyl-2-(4,8,12-
     trimethyltridecyl)-, [2R-[2R*(4R*,8R*)]]-, mixt. contg. (9CI)
FS   STEREOSEARCH
MF   C27 H46 O2 . C18 H37 N O2
CI   MXS
SR   CA
```
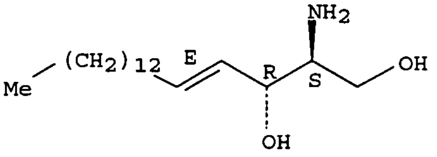

LC STN Files: CA, CAPLUS

CM 1

CRN 123-78-4
CMF C18 H37 N O2

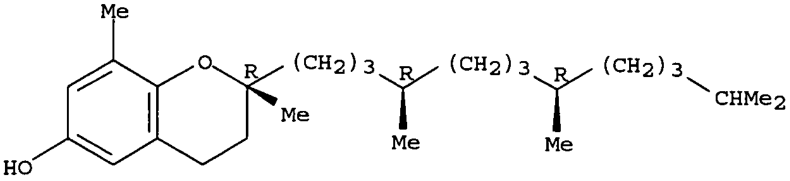
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



CM 2

CRN 119-13-1
CMF C27 H46 O2

Absolute stereochemistry.

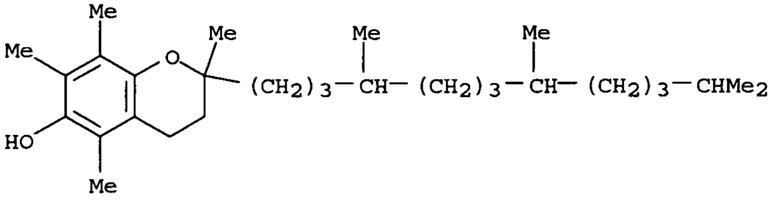


1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 6 OF 24 REGISTRY COPYRIGHT 2005 ACS on STN
RN **153736-66-4** REGISTRY
ED Entered STN: 18 Mar 1994
CN **4-Octadecene-1,3-diol, 2-amino-, [R-[R*,S*-(E)]]-, mixt. with 3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-2H-1-benzopyran-6-ol (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 2H-1-Benzopyran-6-ol, 3,4-dihydro-2,5,7,8-tetramethyl-2-(4,8,12-trimethyltridecyl)-, mixt. contg. (9CI)
FS STEREOSEARCH
MF **C29 H50 O2 . C18 H37 N O2**
CI MXS
SR CA
LC STN Files: CA, CAPLUS

CM 1

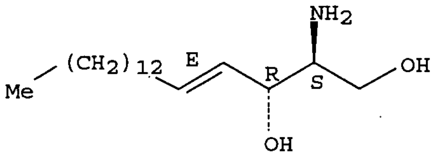
CRN 10191-41-0
CMF C29 H50 O2



CM 2

CRN 123-78-4
CMF C18 H37 N O2

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



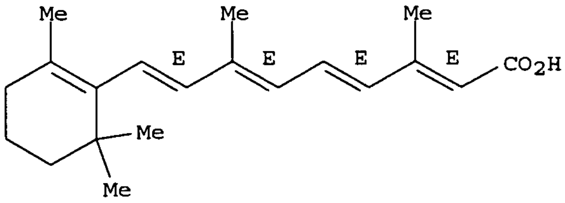
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 7 OF 24 REGISTRY COPYRIGHT 2005 ACS on STN
RN **131660-73-6** REGISTRY
ED Entered STN: 25 Jan 1991
CN **Retinoic acid, mixt. with [R-[R*,S*-(E)]]-2-amino-4-octadecene-1,3-diol (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **4-Octadecene-1,3-diol, 2-amino-, [R-[R*,S*-(E)]]-, mixt. contg. (9CI)**
FS STEREOSEARCH
MF **C20 H28 O2 . C18 H37 N O2**
CI MXS
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 302-79-4
CMF C20 H28 O2

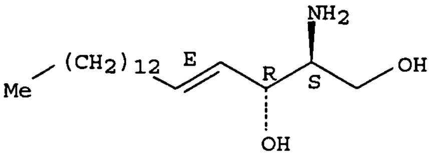
Double bond geometry as shown.



CM 2

CRN 123-78-4

```
     CMF  C18 H37 N O2

Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
```



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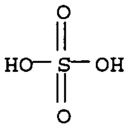
                1 REFERENCES IN FILE CA (1907 TO DATE)
                1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 8 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   131009-80-8  REGISTRY
ED   Entered STN:  14 Dec 1990
CN   4-Octadecene-1,3-diol, 2-amino-, (2S,3R,4E)-, sulfate (salt) (9CI)
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   4-Octadecene-1,3-diol, 2-amino-, [R-[R*,S*-(E)]]-, sulfate (salt)
FS   STEREOSEARCH
MF   C18 H37 N O2 . x H2 O4 S
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT, TOXCENTER, USPATFULL

     CM   1

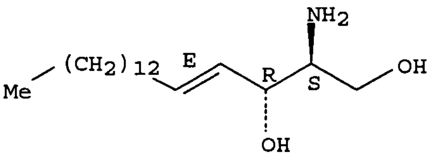
     CRN  7664-93-9
     CMF  H2 O4 S
```



```
     CM   2

     CRN  123-78-4
     CMF  C18 H37 N O2

Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
```



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                2 REFERENCES IN FILE CA (1907 TO DATE)
                2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 9 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   89164-20-5  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, [R-(R*,S*)]- (9CI)  (CA INDEX
     NAME)
```
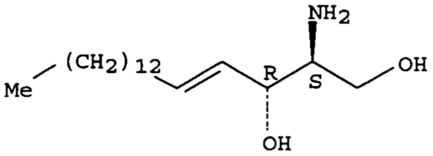

FS STEREOSEARCH
MF **C18 H37 N O2**
LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMINFORMRX
(*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry unknown.

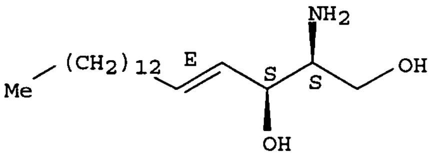


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 10 OF 24 REGISTRY COPYRIGHT 2005 ACS on STN
RN **88494-43-3** REGISTRY
ED Entered STN: 16 Nov 1984
CN **4-Octadecene-1,3-diol, 2-amino-, [R*,R*-(E)]- (9CI)** (CA INDEX NAME)
OTHER NAMES:
CN C18-threo-Sphingenine
CN threo-C18-Sphingenine
FS STEREOSEARCH
DR 2304-77-0
MF **C18 H37 N O2**
CI COM
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER
(*File contains numerically searchable property data)

Relative stereochemistry.
Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

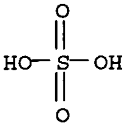
12 REFERENCES IN FILE CA (1907 TO DATE)
12 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 11 OF 24 REGISTRY COPYRIGHT 2005 ACS on STN
RN **56607-20-6** REGISTRY
ED Entered STN: 16 Nov 1984
CN **4-Octadecene-1,3-diol, 2-amino-, (2S,3R,4E)-, sulfate (2:1) (salt) (9CI)** (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN **4-Octadecene-1,3-diol, 2-amino-, [R-[R*,S*-(E)]]-, sulfate (2:1) (salt)**
OTHER NAMES:
CN C18-Sphingosine sulfate
CN Sphingenine sulfate

FS STEREOSEARCH
MF C18 H37 N O2 . 1/2 H2 O4 S
LC STN Files: BIOSIS, CA, CAPLUS, CHEMLIST, CSCHEM, MSDS-OHS, USPATFULL
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

CM 1

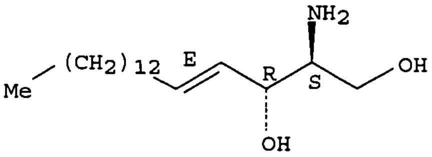
CRN 7664-93-9
CMF H2 O4 S



CM 2

CRN 123-78-4
CMF C18 H37 N O2

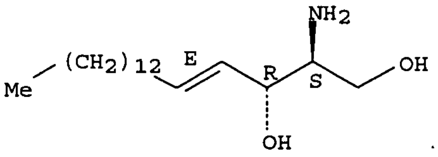
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



6 REFERENCES IN FILE CA (1907 TO DATE)
6 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5 ANSWER 12 OF 24 REGISTRY COPYRIGHT 2005 ACS on STN
RN **35823-65-5** REGISTRY
ED Entered STN: 16 Nov 1984
CN **4-Octadecene-1,3-diol, 2-amino-, hydrobromide, [R-[R*,S*-(E)]]-**
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF **C18 H37 N O2 . Br H**
LC STN Files: CA, CAPLUS
CRN (123-78-4)

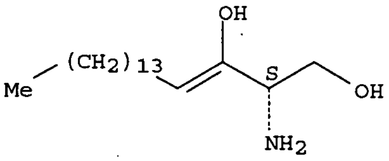
Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



● HBr

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

```
L5   ANSWER 13 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   33047-13-1  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   3-Octadecene-1,3-diol, 2-amino-, (S)- (8CI, 9CI)  (CA INDEX
     NAME)
OTHER NAMES:
CN   (2S)-3-Dehydrosphinganine
FS   STEREOSEARCH
MF   C18 H37 N O2

Absolute stereochemistry.
Double bond geometry unknown.
```



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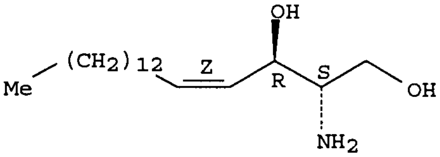
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**


L5   ANSWER 14 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   26308-91-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, (2S,3R,4Z)- (9CI)  (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
CN   4-Octadecene-1,3-diol, 2-amino-, (Z)-D-erythro- (8CI)
CN   4-Octadecene-1,3-diol, 2-amino-, [R-[R*,S*-(Z)]]-
OTHER NAMES:
CN   4,5-cis-Sphingosine
CN   D-(+)-erythro-cis-Sphingosine
FS   STEREOSEARCH
MF   C18 H37 N O2
LC   STN Files:   BEILSTEIN*, CA, CAPLUS, CASREACT, CHEMINFORMRX, TOXCENTER,
       USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
```



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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              16 REFERENCES IN FILE CA (1907 TO DATE)
              16 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 15 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   25695-95-8  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, (2S,3S,4E)- (9CI)  (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
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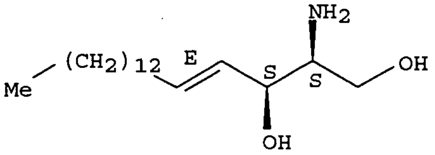
```
CN   4-Octadecene-1,3-diol, 2-amino-, (E)-L-threo- (8CI)
CN   4-Octadecene-1,3-diol, 2-amino-, [S-[R*,R*-(E)]]-
OTHER NAMES:
CN   (2S,3S)-Sphingosine
CN   3-L-4-Sphingenine
CN   L-threo-C18-Sphingosine
CN   L-threo-Sphingosine
FS   STEREOSEARCH
DR   31956-53-3, 246245-50-1
MF   C18 H37 N O2
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMINFORMRX,
       TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry as shown.
```



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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               58 REFERENCES IN FILE CA (1907 TO DATE)
                1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
               58 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 16 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   19316-52-0  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, hydrochloride, [R*,S*-(E)]- (9CI)
     (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   4-Octadecene-1,3-diol, 2-amino-, hydrochloride, [R*,S*-(E)]-(±)-

FS   STEREOSEARCH
MF   C18 H37 N O2 . Cl H
CRN  (2733-29-1)

Relative stereochemistry.
Double bond geometry as shown.
```

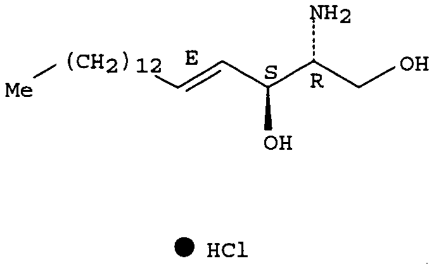

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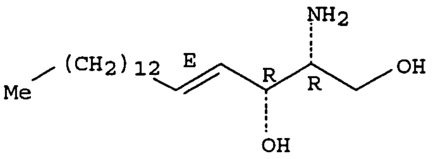
L5   ANSWER 17 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   6036-85-7  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, (2R,3R,4E)- (9CI)  (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
```

```
CN   4-Octadecene-1,3-diol, 2-amino-, (E)-D-threo- (8CI)
CN   4-Octadecene-1,3-diol, 2-amino-, [R-[R*,R*-(E)]]-
OTHER NAMES:
CN   D-threo-C18-Sphingosine
CN   D-threo-Sphingosine
CN   threo-C18-Sphingosine
FS   STEREOSEARCH
MF   C18 H37 N O2
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,
       CHEMINFORMRX, CSCHEM, TOXCENTER, USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.
Double bond geometry as shown.
```



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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              35 REFERENCES IN FILE CA (1907 TO DATE)
              35 REFERENCES IN FILE CAPLUS (1907 TO DATE)
               2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L5   ANSWER 18 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   6036-75-5  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, (2R,3S,4E)- (9CI)  (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
CN   4-Octadecene-1,3-diol, 2-amino-, [S-[R*,S*-(E)]]-
OTHER NAMES:
CN   L-erythro-C18-Sphingosine
CN   L-erythro-Sphingosine
FS   STEREOSEARCH
MF   C18 H37 N O2
LC   STN Files:   BEILSTEIN*, BIOSIS, CA, CAPLUS, CASREACT, CHEMCATS,
       CHEMINFORMRX, CSCHEM, TOXCENTER, USPAT2, USPATFULL
         (*File contains numerically searchable property data)

Absolute stereochemistry.  Rotation (+).
Double bond geometry as shown.
```
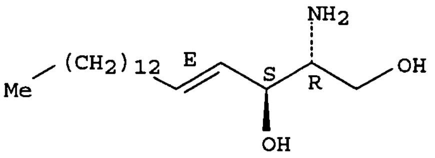
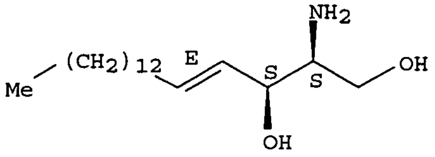
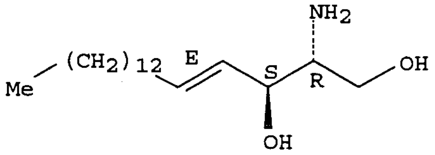



```
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              37 REFERENCES IN FILE CA (1907 TO DATE)
              37 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L5   ANSWER 19 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   4363-88-6  REGISTRY
ED   Entered STN:  16 Nov 1984
```

```
CN    4-Octadecene-1,3-diol, 2-amino-, labeled with tritium, [R*,R*-(E)]-
      (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN    4-Octadecene-1,3-diol, 2-amino-, labeled with tritium,
      [R*,R*-(E)]-(±)-
FS    STEREOSEARCH
MF    C18 H37 N O2
IL    XH-3

Relative stereochemistry.
Double bond geometry as shown.
```



```
L5    ANSWER 20 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN    4358-27-4  REGISTRY
ED    Entered STN:  16 Nov 1984
CN    4-Octadecene-1,3-diol, 2-amino-, labeled with tritium, [R*,S*-(E)]-
      (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN    4-Octadecene-1,3-diol, 2-amino-, labeled with tritium, DL-erythro-
      (8CI)
CN    4-Octadecene-1,3-diol, 2-amino-, labeled with tritium,
      [R*,S*-(E)]-(±)-
FS    STEREOSEARCH
MF    C18 H37 N O2
IL    XH-3

Relative stereochemistry.
Double bond geometry as shown.
```



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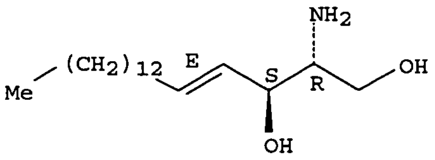
L5    ANSWER 21 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN    2733-29-1  REGISTRY
ED    Entered STN:  16 Nov 1984
CN    4-Octadecene-1,3-diol, 2-amino-, (2R,3S,4E)-rel- (9CI)   (CA
      INDEX NAME)
OTHER CA INDEX NAMES:
CN    4-Octadecene-1,3-diol, 2-amino-, (E)-DL-erythro- (8CI)
CN    4-Octadecene-1,3-diol, 2-amino-, [R*,S*-(E)]-(±)-
OTHER NAMES:
CN    4-Octadecene-1,3-diol, 2-amino-, [R*,S*-(E)]-
CN    C18-erythro-Sphingenine
CN    DL-erythro-Sphingosine
CN    erythro-C18-Sphingenine
CN    Erythro-DL-Sphingosine
FS    STEREOSEARCH
DR    88494-42-2
MF    C18 H37 N O2
CI    COM
LC    STN Files:   BEILSTEIN*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,
        CHEMINFORMRX, SPECINFO, TOXCENTER, USPATFULL
          (*File contains numerically searchable property data)

Relative stereochemistry.
Double bond geometry as shown.
```



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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

             30 REFERENCES IN FILE CA (1907 TO DATE)
              1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             30 REFERENCES IN FILE CAPLUS (1907 TO DATE)
              1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L5   ANSWER 22 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   2673-72-5  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, hydrochloride, [R-[R*,S*-(E)]]-
     (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   4-Octadecene-1,3-diol, 2-amino-, hydrochloride, (E)-D-erythro-
     (8CI)
OTHER NAMES:
CN   D-erythro-1,3-Dihydroxy-2-amino-trans-4-octadecene hydrochloride
FS   STEREOSEARCH
MF   C18 H37 N O2 . Cl H
LC   STN Files:   CA, CAOLD, CAPLUS
CRN  (123-78-4)

Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
```
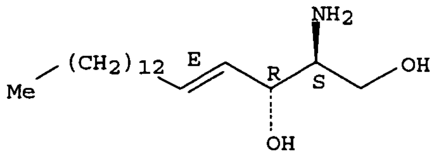
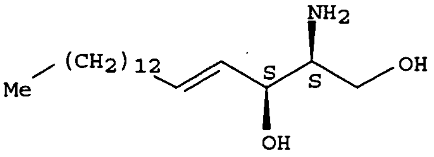



● HCl

```
              3 REFERENCES IN FILE CA (1907 TO DATE)
              3 REFERENCES IN FILE CAPLUS (1907 TO DATE)
              1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L5   ANSWER 23 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   871-45-4  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, (R*,R*)- (9CI)  (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN   4-Octadecene-1,3-diol, 2-amino-, threo- (8CI)
FS   STEREOSEARCH
MF   C18 H37 N O2
LC   STN Files:   BEILSTEIN*, CA, CAOLD, CAPLUS, CHEMINFORMRX
          (*File contains numerically searchable property data)
```

Relative stereochemistry.
Double bond geometry unknown.



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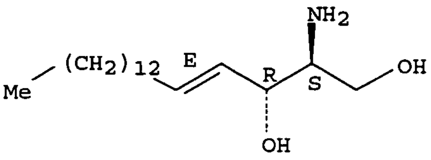
**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

               2 REFERENCES IN FILE CA (1907 TO DATE)
               2 REFERENCES IN FILE CAPLUS (1907 TO DATE)
               2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L5   ANSWER 24 OF 24  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   123-78-4  REGISTRY
ED   Entered STN:  16 Nov 1984
CN   4-Octadecene-1,3-diol, 2-amino-, (2S,3R,4E)- (9CI)  (CA INDEX
     NAME)
OTHER CA INDEX NAMES:
CN   4-Octadecene-1,3-diol, 2-amino-, (E)-D-erythro- (8CI)
CN   4-Octadecene-1,3-diol, 2-amino-, [R-[R*,S*-(E)]]-
OTHER NAMES:
CN   (-)-D-erythro-Sphingosine
CN   (2S,3R)-Sphingosine
CN   (2S,3R,4E)-2-Amino-4-octadecene-1,3-diol
CN   (4E)-Sphingenine
CN   4-Sphingenine
CN   4-trans-Sphingenine
CN   C18-Sphingosine
CN   D-(+)-erytho-4-trans-Sphingenine
CN   D-erythro-C18-Sphingosine
CN   D-erythro-Sphingosine
CN   D-Sphingosine
CN   erythro-4-Sphingenine
CN   erythro-C18-Sphingosine
CN   Erythrosphingosine
CN   Sphingenine
CN   Sphingosine
CN   trans-4-Sphingenine
FS   STEREOSEARCH
DR   45261-75-4
MF   C18 H37 N O2
CI   COM
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
       BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CEN, CHEMCATS,
       CHEMINFORMRX, CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIUDB,
       IPA, MEDLINE, MRCK*, NAPRALERT, PROMT, SYNTHLINE, TOXCENTER, USPAT2,
       USPATFULL
         (*File contains numerically searchable property data)
     Other Sources:   EINECS**
         (**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
```



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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

            1154 REFERENCES IN FILE CA (1907 TO DATE)
              67 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            1160 REFERENCES IN FILE CAPLUS (1907 TO DATE)
              19 REFERENCES IN FILE CAOLD (PRIOR TO 1967)


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L8   ANSWER 1 OF 6  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   313354-16-4  REGISTRY
ED   Entered STN:  10 Jan 2001
CN   Adenosine 5'-(tetrahydrogen triphosphate-P-33P), compd. with
     N,N-diethylethanamine (1:4) (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C10 H16 N5 O13 P3 . 4 C6 H15 N
SR   CAS Client Services
LC   STN Files:   CHEMCATS

     CM   1

     CRN  133587-39-0
     CMF  C10 H16 N5 O13 P3

Absolute stereochemistry.
```

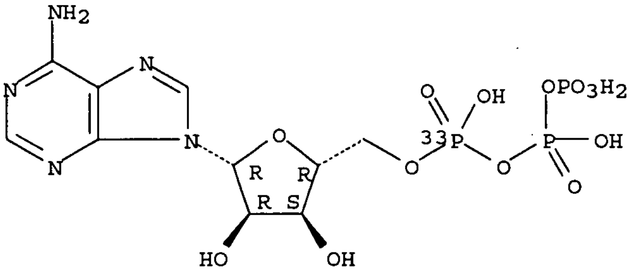

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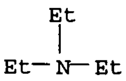
     CM   2

     CRN  121-44-8
     CMF  C6 H15 N
```



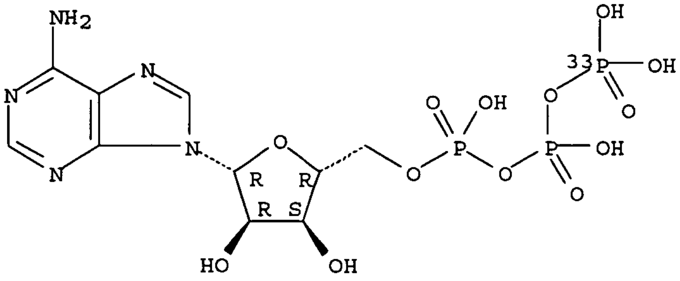
```
L8   ANSWER 2 OF 6  REGISTRY  COPYRIGHT 2005 ACS on STN
RN   313263-38-6  REGISTRY
ED   Entered STN:  09 Jan 2001
```

```
CN     Adenosine 5'-(tetrahydrogen triphosphate-P''-33P), compd. with
       N,N-diethylethanamine (1:4) (9CI)  (CA INDEX NAME)
FS     STEREOSEARCH
MF     C10 H16 N5 O13 P3 . 4 C6 H15 N
SR     CAS Client Services
LC     STN Files:   CHEMCATS

       CM   1

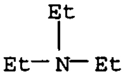
       CRN  133587-41-4
       CMF  C10 H16 N5 O13 P3

Absolute stereochemistry.
```



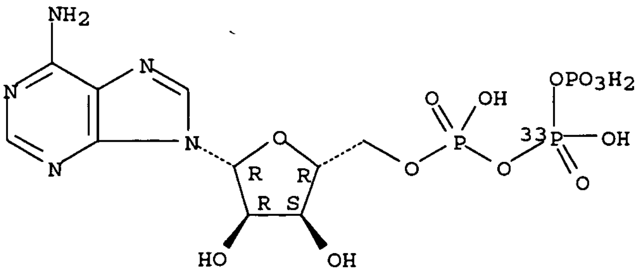
```
       CM   2

       CRN  121-44-8
       CMF  C6 H15 N
```



```
L8     ANSWER 3 OF 6  REGISTRY  COPYRIGHT 2005 ACS on STN
RN     223754-89-0  REGISTRY
ED     Entered STN:  28 May 1999
CN     Adenosine 5'-(tetrahydrogen triphosphate-P'-33P) (9CI)  (CA
       INDEX NAME)
FS     STEREOSEARCH
MF     C10 H16 N5 O13 P3
SR     CA
LC     STN Files:   CA, CAPLUS

Absolute stereochemistry.
```

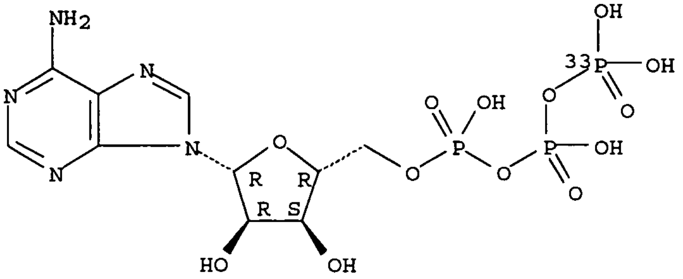


```
                 1 REFERENCES IN FILE CA (1907 TO DATE)
```

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L8 ANSWER 4 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN
RN 133587-41-4 REGISTRY
ED Entered STN: 03 May 1991
CN **Adenosine 5'-(tetrahydrogen triphosphate-P''-33P) (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C10 H16 N5 O13 P3**
CI COM
SR CA
LC STN Files: CA, CAPLUS, CASREACT, CHEMCATS, TOXCENTER, USPAT2, USPATFULL

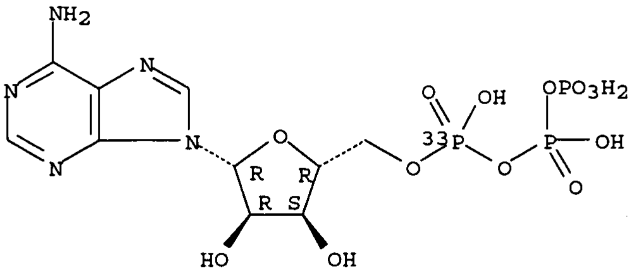
Absolute stereochemistry.



22 REFERENCES IN FILE CA (1907 TO DATE)
22 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L8 ANSWER 5 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN
RN 133587-39-0 REGISTRY
ED Entered STN: 03 May 1991
CN **Adenosine 5'-(tetrahydrogen triphosphate-P-33P) (9CI)** (CA INDEX NAME)
FS STEREOSEARCH
MF **C10 H16 N5 O13 P3**
CI COM
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

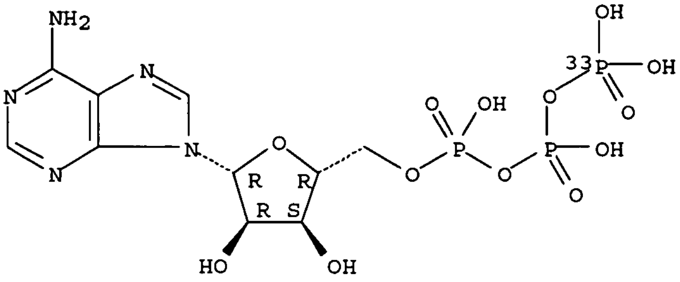


2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L8 ANSWER 6 OF 6 REGISTRY COPYRIGHT 2005 ACS on STN
RN 65733-38-2 REGISTRY
ED Entered STN: 16 Nov 1984
CN **Adenosine 5'-(tetrahydrogen triphosphate-P''-33P), tetraammonium salt (9CI)** (CA INDEX NAME)
FS STEREOSEARCH

```
MF    C10 H16 N5 O13 P3 . 4 H3 N
LC    STN Files:   CA, CAPLUS
CRN   (133587-41-4)

Absolute stereochemistry.
```



```
                    ●4  NH3

               1 REFERENCES IN FILE CA (1907 TO DATE)
               1 REFERENCES IN FILE CAPLUS (1907 TO DATE)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     (FILE 'HOME' ENTERED AT 07:48:28 ON 23 JUN 2005)

     FILE 'REGISTRY' ENTERED AT 07:48:54 ON 23 JUN 2005
                ACT GIT485LIP1/A
               ---------
L1   (       423)SEA ABB=ON  PLU=ON  C18H37NO2
L2               QUE ABB=ON  PLU=ON  (PMS OR MAN OR IDS)/CI OR UNSPECIFIED OR
                COMPD OR COMPOUND OR (D OR T)/ELS
L3   (       364)SEA ABB=ON  PLU=ON  L1 NOT L2
L4   (        36)SEA ABB=ON  PLU=ON  L3 AND 1(1A)3(1A)DIOL AND 2 (1A)AMIN?
L5            24 SEA ABB=ON  PLU=ON  L4 AND (123-78-4/BI OR 131009-80-8/BI OR
                131660-73-6/BI OR 153736-66-4/BI OR 153736-67-5/BI OR 153736-68
                -6/BI OR 157240-87-4/BI OR 19316-52-0/BI OR 207516-16-3/BI OR
                25695-95-8/BI OR 26308-91-8/BI OR 2673-72-5/BI OR 2733-29-1/BI
                OR 291762-73-7/BI OR 33047-13-1/BI OR 35823-65-5/BI OR
                4358-27-4/BI OR 4363-88-6/BI OR 56607-20-6/BI OR 6036-75-5/BI
                OR 6036-85-7/BI OR 871-45-4/BI OR 88494-43-3/BI OR 89164-20-5/B
                I)
               ---------
                ACT GIT485ENZ1/A
               ---------
L6            97 SEA ABB=ON  PLU=ON  SPHINGOSIN? (1A)KINASE?
               ---------
                ACT GIT485C41/A
               ---------
L7   (       528)SEA ABB=ON  PLU=ON  C10H16N5O13P3
L8             6 SEA ABB=ON  PLU=ON  L7 AND (P33 OR 33P)
               ---------

     FILE 'HCAPLUS' ENTERED AT 07:50:46 ON 23 JUN 2005
                ACT GITLIPR/A
               ---------
L9   (     20433)SEA ABB=ON  PLU=ON  (LIPIDS+OLD,NT1/CT OR LIPID#/CW) (L)
                RACT+NT/RL
L10  (     21342)SEA ABB=ON  PLU=ON  FATTY ACIDS+NT/CT (L)RACT+NT/RL
L11  (      2716)SEA ABB=ON  PLU=ON  GLYCERIDES+NT/CT (L)RACT+NT/RL
L12  (      2510)SEA ABB=ON  PLU=ON  GLYCOLIPIDS+OLD,NT/CT(L)RACT+NT/RL
```

```
L13 (       5696)SEA ABB=ON  PLU=ON  PHOSPHOLIPIDS+OLD,NT/CT(L)RACT+NT/RL
L14 (          5)SEA ABB=ON  PLU=ON  PROTEOLIPIDS+OLD,NT/CT (L) RACT+NT/RL
L15 (      18697)SEA ABB=ON  PLU=ON  STEROIDS+NT/CT (L) RACT+NT/RL
L16 (         36)SEA ABB=ON  PLU=ON  SULFOLIPIDS+NT/CT (L) RACT+NT/RL
L17 (      24131)SEA ABB=ON  PLU=ON  TERPENES+OLD,NT/CT(L) RACT+NT/RL
L18 (        141)SEA ABB=ON  PLU=ON  SPHINGOSINE/CT (L) RACT+NT/RL
L19          74279 SEA ABB=ON  PLU=ON  (L9 OR L10 OR L11 OR L12 OR L13 OR L14 OR
                   L15 OR L16 OR L17 OR L18)
                  ---------
L20           6859 SEA ABB=ON  PLU=ON  L5 OR 4(1A)OCTADECEN? (1A) 1(1A)3(1A)DIOL
                   (1A)2(1A)AMINO OR ?SPHING!!INE OR 1(1A)3 (1A)(DIHYDROXY OR
                   DI(1A)HYDROXY) (1A)2(1A)AMINO (1A)4(1A)OCTADECEN?
L21            431 SEA ABB=ON  PLU=ON  L20 (L) RACT+NT/RL
L22           1620 SEA ABB=ON  PLU=ON  (L19 OR L20 OR L21) AND ANT/RL
L23          19747 SEA ABB=ON  PLU=ON  ((JOHNS? OR J) (1A) (JOHNS? OR J))/CS,PA
                   E GAMBLE J/AU
L24            182 SEA ABB=ON  PLU=ON  ("GAMBLE J"/AU OR "GAMBLE J A"/AU OR
                   "GAMBLE J A S"/AU OR "GAMBLE J C"/AU OR "GAMBLE J D"/AU OR
                   "GAMBLE J F"/AU OR "GAMBLE J L"/AU OR "GAMBLE J L JR"/AU OR
                   "GAMBLE J R"/AU OR "GAMBLE J T"/AU OR "GAMBLE J W"/AU OR
                   "GAMBLE JENNIFER"/AU OR "GAMBLE JENNIFER R"/AU OR "GAMBLE
                   JENNIFER RUTH"/AU OR "GAMBLE JENNY"/AU OR "GAMBLE JENNY R"/AU)
                   E VADAS M/AU
L25            207 SEA ABB=ON  PLU=ON  ("VADAS M"/AU OR "VADAS M A"/AU OR "VADAS
                   MATHEW"/AU OR "VADAS MATHEW A"/AU OR "VADAS MATHEW ALEXANDER"/A
                   U OR "VADAS MATTHEW"/AU OR "VADAS MATTHEW A"/AU)
                   E XIA P/AU
L26             41 SEA ABB=ON  PLU=ON  ("XIA P"/AU OR "XIA P C"/AU OR "XIA P
                   F"/AU OR "XIA P J"/AU OR "XIA P W"/AU)
                   E XIA PU/AU
L27             42 SEA ABB=ON  PLU=ON  "XIA PU"/AU
                   E BARTER P/AU
L28            178 SEA ABB=ON  PLU=ON  ("BARTER P"/AU OR "BARTER P I"/AU OR
                   "BARTER P J"/AU OR "BARTER P R"/AU OR "BARTER PHILIP"/AU OR
                   "BARTER PHILIP J"/AU OR "BARTER PHILLIP"/AU OR "BARTER PHILLIP
                   J"/AU)
                   E RYE K/AU
L29             83 SEA ABB=ON  PLU=ON  ("RYE K"/AU OR "RYE K A"/AU OR "RYE K
                   W"/AU OR "RYE KERRY ANN"/AU OR "RYE KERRY ANNE"/AU)
                   E WATTENBERG B/AU
L30              8 SEA ABB=ON  PLU=ON  ("WATTENBERG B"/AU OR "WATTENBERG B W"/AU
                   OR "WATTENBERG BRIAN"/AU OR "WATTENBERG BRIAN W"/AU OR
                   "WATTENBERG BRIAN WOLFF"/AU)
                   E PITSON S/AU
L31             40 SEA ABB=ON  PLU=ON  ("PITSON S"/AU OR "PITSON S M"/AU OR
                   "PITSON STUART"/AU OR "PITSON STUART M"/AU OR "PITSON STUART
                   MAXWELL"/AU)
L32              3 SEA ABB=ON  PLU=ON  L22 AND (L24 OR L25 OR L26 OR L27 OR L28
                   OR L29 OR L30 OR L31)
L33              1 SEA ABB=ON  PLU=ON  L22 AND L23
L34                QUE ABB=ON  PLU=ON  (IMMUNOASSAY+OLD,NT OR LAB-ON-A-CHIP+NT)/CT
                   E IMMUNOASSAY/CT
                   E E3+ALL
                   E BIOCHIP/CT
                   E E5+ALL
                   E E7
                   E E3+ALL
                   E MICROARRAY TECHNOLOGY/CT
                   E E3+ALL
L35          15973 SEA ABB=ON  PLU=ON  (BIOCHIPS OR BIOSENSORS OR CLINICAL
                   ANALYZERS+NT)/CT
                   E ANALYTICAL APPARATUS/CT
                   E E3+ALL
L36            163 SEA ABB=ON  PLU=ON  ANALYTICAL APPARATUS+OLD,NT/CT (L)
                   MICROARRAY
L37          34221 SEA ABB=ON  PLU=ON  DRUG SCREENING +OLD,NT/CT
```

```
                E HIGH THROUGHPUT SCREENING/CT
                E E3+ALL
L38        5094 SEA ABB=ON  PLU=ON  HIGH THROUGHPUT SCREENING/CT
L39       59210 SEA ABB=ON  PLU=ON  ANALYS!S/CW (L) (MICRO? OR APP?)
L40        1617 SEA ABB=ON  PLU=ON  L22 NOT L32
L41         235 SEA ABB=ON  PLU=ON  L40 AND (L34 OR L35 OR L36 OR L37 OR L38
                OR L39)
                E RADILABEL/CT
                E RADIOLABEL/CT
                E E5+ALL
                E E2
                E E3+ALL
L42             QUE ABB=ON  PLU=ON  ISOTOPOMERS+OLD,NT/CT
                E RADIOISOTOPE/CT
                E RADIOISOTOPES/CT
                E E+ALL
                E ISOTOPES/CT
                E E3+ALL
L43             QUE ABB=ON  PLU=ON  ISOTOPES+OLD,NT/CT
                E E333
                E E3+ALL
L44        7331 SEA ABB=ON  PLU=ON  ISOTOPE INDICATORS/CT
                E RADIOISOTOPES/CT
                E E10
                E E3+ALL
                E DNA/CT
                E NUCLEIC ACIDS/CT
                E E3+ALL
L45             QUE ABB=ON  PLU=ON  NUCLEIC ACIDS+OLD,NT/CT (L) (?LABEL? OR
                ?MARK? OR TAGG? OR ?ISOTOP?) (L) ANT/RL
                E TEST KITS/CT
                E E3+ALL
L46       13770 SEA ABB=ON  PLU=ON  TEST KITS/CT
L47          52 SEA ABB=ON  PLU=ON  L46 AND L40
L48         252 SEA ABB=ON  PLU=ON  L41 OR L47
L49          15 SEA ABB=ON  PLU=ON  L48 AND (L42 OR L43 OR L44 OR L45)
L50             QUE ABB=ON  PLU=ON  PY<=1998 OR AY<=1998 OR PRY<=1998 OR
                PD<19980908 OR AD<19980908 OR PRD<19980908
L51           4 SEA ABB=ON  PLU=ON  L49 AND L50
L52           3 SEA ABB=ON  PLU=ON  ("126:57117"/AN OR "131:181953"/AN OR
                "136:275646"/AN OR "1997:34059"/AN OR "1999:565880"/AN OR
                "2002:241288"/AN) AND L51
                D AB TOT
                D SCA
                D TI TOT
                SEL AN 1-2
L53           2 SEA ABB=ON  PLU=ON  ("131:181953"/AN OR "136:275646"/AN OR
                "1999:565880"/AN OR "2002:241288"/AN) AND L52
L54          10 SEA ABB=ON  PLU=ON  L48 AND (L42 OR L43 OR L44)
L55           3 SEA ABB=ON  PLU=ON  L54 AND L50
L56          40 SEA ABB=ON  PLU=ON  L40 AND (L42 OR L43 OR L44 OR L45)
L57          23 SEA ABB=ON  PLU=ON  L56 AND L50
L58          79 SEA ABB=ON  PLU=ON  (L19 OR L20 OR L21) AND (ANT/RL (L)(?LABEL?
                 OR ?MARK? OR ?TAGG? OR ?ISOTOP?))
L59           0 SEA ABB=ON  PLU=ON  L58 AND (L23 OR L24 OR L25 OR L26 OR L27
                OR L28 OR L29 OR L30 OR L31)
L60          39 SEA ABB=ON  PLU=ON  L58 AND L50
L61          56 SEA ABB=ON  PLU=ON  L57 OR L60
L62          12 SEA ABB=ON  PLU=ON  ("121:246531"/AN OR "125:81261"/AN OR
                "126:86792"/AN OR "128:280452"/AN OR "129:145261"/AN OR
                "131:181953"/AN OR "132:162808"/AN OR "136:275646"/AN OR
                "1976:587540"/AN OR "1978:185637"/AN OR "1978:47246"/AN OR
                "1981:528686"/AN OR "1994:646531"/AN OR "1996:323936"/AN OR
                "1997:85099"/AN OR "1998:269349"/AN OR "1998:373958"/AN OR
                "1999:565880"/AN OR "2000:95952"/AN OR "2002:241288"/AN OR
                "85:187540"/AN OR "88:185637"/AN OR "88:47246"/AN OR "95:128686
                "/AN) AND L61
L63          11 SEA ABB=ON  PLU=ON  ("125:81261"/AN OR "126:86792"/AN OR
                "128:280452"/AN OR "129:145261"/AN OR "131:181953"/AN OR
                "132:162808"/AN OR "136:275646"/AN OR "1976:587540"/AN OR
                "1978:185637"/AN OR "1978:47246"/AN OR "1981:528686"/AN OR
                "1996:323936"/AN OR "1997:85099"/AN OR "1998:269349"/AN OR
                "1998:373958"/AN OR "1999:565880"/AN OR "2000:95952"/AN OR
                "2002:241288"/AN OR "85:187540"/AN OR "88:185637"/AN OR
                "88:47246"/AN OR "95:128686"/AN) AND L62
L64          11 SEA ABB=ON  PLU=ON  L53 OR L55 OR L63

     FILE 'BIOSIS' ENTERED AT 09:28:01 ON 23 JUN 2005
L65       69853 SEA ABB=ON  PLU=ON  (?LIPID? OR L20 OR FAT? (1A) ACID? OR
                OIL?) AND (?LABEL? OR ?MARK? OR ?TAGG? OR ?ISOTOP?)
L66       21530 SEA ABB=ON  PLU=ON  L65 AND (DETECT? OR ANALAYTE? OR DETERMIN?)
L67       22674 SEA ABB=ON  PLU=ON  ((JOHNS? OR J) (1A) (JOHNS? OR J))/CS
L68          11 SEA ABB=ON  PLU=ON  L66 AND L67
                D BIB TOT
                E GAMBLE J/AU
L69         342 SEA ABB=ON  PLU=ON  ("GAMBLE J"/AU OR "GAMBLE J A"/AU OR
                "GAMBLE J A S"/AU OR "GAMBLE J B"/AU OR "GAMBLE J C"/AU OR
                "GAMBLE J E"/AU OR "GAMBLE J F"/AU OR "GAMBLE J G"/AU OR
                "GAMBLE J L"/AU OR "GAMBLE J L JR"/AU OR "GAMBLE J M"/AU OR
                "GAMBLE J N"/AU OR "GAMBLE J R"/AU OR "GAMBLE J S"/AU OR
                "GAMBLE J T"/AU OR "GAMBLE J W"/AU)
                E GAMBLE JEN/AU
L70          55 SEA ABB=ON  PLU=ON  ("GAMBLE JENNIFER"/AU OR "GAMBLE JENNIFER
                R"/AU OR "GAMBLE JENNY"/AU OR "GAMBLE JENNY R"/AU)
                E VADAS M/AU
L71         324 SEA ABB=ON  PLU=ON  ("VADAS M"/AU OR "VADAS M A"/AU OR "VADAS
                MATHEW"/AU OR "VADAS MATHEW A"/AU OR "VADAS MATHEW ALEXANDER"/A
                U OR "VADAS MATTHEW"/AU OR "VADAS MATTHEW A"/AU)
                E XIA P/AU
L72          55 SEA ABB=ON  PLU=ON  ("XIA P"/AU OR "XIA P Y"/AU)
                E XIA PU/AU
L73          20 SEA ABB=ON  PLU=ON  "XIA PU"/AU
                E BARTER P/AU
L74         187 SEA ABB=ON  PLU=ON  ("BARTER P"/AU OR "BARTER P I"/AU OR
                "BARTER P J"/AU OR "BARTER PAUL J"/AU OR "BARTER PHILIP"/AU OR
                "BARTER PHILIP J"/AU OR "BARTER PHILIPPA"/AU OR "BARTER
                PHILLIP"/AU)
                E RYE K/AU
L75          69 SEA ABB=ON  PLU=ON  ("RYE K"/AU OR "RYE K A"/AU OR "RYE KERRY
                ANN"/AU OR "RYE KERRY ANNE"/AU)
                E WATTENBERG B/AU
L76          30 SEA ABB=ON  PLU=ON  ("WATTENBERG B"/AU OR "WATTENBERG B W"/AU
                OR "WATTENBERG BRIAN"/AU)
                E PITSON S/AU
L77          35 SEA ABB=ON  PLU=ON  ("PITSON S"/AU OR "PITSON S M"/AU OR
                "PITSON STUART"/AU OR "PITSON STUART M"/AU)
L78           0 SEA ABB=ON  PLU=ON  L67 AND (L69 OR L70 OR L71 OR L72 OR L73
                OR L74 OR L75 OR L76 OR L77)
L79          35 SEA ABB=ON  PLU=ON  L65 AND (L69 OR L70 OR L71 OR L72 OR L73
                OR L74 OR L75 OR L76 OR L77)
L80          12 SEA ABB=ON  PLU=ON  L79 AND CELL?

     FILE 'HCAPLUS' ENTERED AT 09:52:51 ON 23 JUN 2005
L81          99 SEA ABB=ON  PLU=ON  L8 OR (ATP OR ADENOSINE (2A)(TETRAHYDROGEN
                OR TETRA (1A)HYDROGEN) (1A)(TRIPHOSPHATE OR TRI(1A)PHOSPHATE))(
                1A)33P
L82           1 SEA ABB=ON  PLU=ON  L81 AND L20
L83       18545 SEA ABB=ON  PLU=ON  L6 OR 4(1A)OCTADECEN? (1A)1(1A)3(1A)DIOL
                (1A)2(1A)AMINO OR ?SPHING!!INE OR 1(1A)3(1A)(DIHYDROXY OR
                DI(1A)HYDROXY) (1A)2(1A)AMINO (1A)4(1A)OCTADECEN? OR ERK OR
                ERK (1A) KINASE
L84       31464 SEA ABB=ON  PLU=ON  (MAP OR MITOGEN? (1A)ACTIVAT? (1A)(PROTEIN?
               OR ?PEPTID?) OR EXTRACELL? (1A)SIGNAL? (1A)REGULAT?) (1A)
              KINASE? OR MAPK
L85         349 SEA ABB=ON  PLU=ON  (L83 OR L84)(L)ANT/RL
L86           2 SEA ABB=ON  PLU=ON  L85 AND L81
L87         128 SEA ABB=ON  PLU=ON  L85 AND L20
L88         431 SEA ABB=ON  PLU=ON  L20 (L) RACT+NT/RL
L89           8 SEA ABB=ON  PLU=ON  L88 AND L85
L90          10 SEA ABB=ON  PLU=ON  L86 OR L89
L91          10 SEA ABB=ON  PLU=ON  L82 OR L90
L92           1 SEA ABB=ON  PLU=ON  L91 AND (L23 OR L24 OR L25 OR L26 OR L27
              OR L28 OR L29 OR L30 OR L31)
L93           9 SEA ABB=ON  PLU=ON  L91 NOT L92
L94           3 SEA ABB=ON  PLU=ON  L32 OR L92
L95          20 SEA ABB=ON  PLU=ON  L64 OR L93

     FILE 'WPIX' ENTERED AT 10:20:29 ON 23 JUN 2005
L96         546 SEA ABB=ON  PLU=ON  (4(1A)OCTADECEN? (1A)1(1A)3(1A)DIOL
              (1A)2(1A)AMINO OR ?SPHING!!INE OR 1(1A)3(1A)(DIHYDROXY OR
              DI(1A)HYDROXY) (1A)2(1A)AMINO (1A)4(1A)OCTADECEN?)/BIX
L97       31465 SEA ABB=ON  PLU=ON  C11C/IPC OR (B04-B01## OR C04-B01## OR
              D03-F07)/MC OR (V795 OR V796 OR V77# OR V780)/MC
L98       19776 SEA ABB=ON  PLU=ON  C07B059/IPC OR (E05-R OR B05-A04 OR
              C05-A04 OR E11-Q03K OR K09-E)/MC OR (C811 OR C812 OR R513)/M0,M
              1,M2,M3,M4,M5,M6
              E SPINGOSINE/DRN
              E SPHINGOSINE/DRN
              E SPHINGOSINE/DCN
              E E3
              E E3+ALL
L99          86 SEA ABB=ON  PLU=ON  R06738/DCN
              E SPHINGOSINE/CN
L100          2 SEA ABB=ON  PLU=ON  SPHINGOSINE/CN
L101          2 SEA ABB=ON  PLU=ON  (RA0V7A/SDCN OR R06738/SDCN)
              D QUE L83
L102        799 SEA ABB=ON  PLU=ON  (4(1A)OCTADECEN?(1A)1(1A)3(1A)DIOL
              (1A)2(1A)AMINO OR ?SPHING!!INE OR 1(1A)3(1A)(DIHYDROXY OR
              DI(1A)HYDROXY) (1A)2(1A)AMINO (1A)4(1A)OCTADECEN? OR ERK OR
              ERK (1A) KINASE?)/BIX
              D QUE L84
L103        893 SEA ABB=ON  PLU=ON  ((MAP OR MITOGEN? (1A)ACTIVAT?(1A)(PROTEIN?
               OR ?PEPTID?) OR EXTRACELL? (1A)SIGNAL? (1A)REGULAT?) (1A)
              KINASE? OR MAPK)/BIX
              E SPHINGOSINE KINASE/DRN
              E SPHINGOSINE KINASE/DCN
              E SPHINGOSINE KINASE/CN
L104          1 SEA ABB=ON  PLU=ON  SPHINGOSINE-KINASE/CN
              SEL SDCN
L105          1 SEA ABB=ON  PLU=ON  RABL9D/SDCN
L106       6082 SEA ABB=ON  PLU=ON  R63#/M0,M1,M2,M3,M4,M5,M6 AND L98
L107            QUE ABB=ON  PLU=ON  G01N033/IPC OR (S03-E14H? OR B11-C08? OR
              C11-C08? OR C11-C10? OR B11-C10? OR D05-H?)/MC
L108      30203 SEA ABB=ON  PLU=ON  ((JOHNS? OR J) (1A) (JOHNS? OR J))/CS,PA
              E GAMBLE J/AU
L109         60 SEA ABB=ON  PLU=ON  ("GAMBLE J"/AU OR "GAMBLE J A"/AU OR
              "GAMBLE J B"/AU OR "GAMBLE J D"/AU OR "GAMBLE J E"/AU OR
              "GAMBLE J F"/AU OR "GAMBLE J G"/AU OR "GAMBLE J J"/AU OR
              "GAMBLE J L"/AU OR "GAMBLE J M"/AU OR "GAMBLE J R"/AU OR
              "GAMBLE J S"/AU OR "GAMBLE J W"/AU)
              E VADAS M/AU
L110         21 SEA ABB=ON  PLU=ON  ("VADAS M"/AU OR "VADAS M A"/AU)
              E XIA P/AU
L111         43 SEA ABB=ON  PLU=ON  ("XIA P"/AU OR "XIA P X"/AU)
              E BARTER P/AU
L112          3 SEA ABB=ON  PLU=ON  ("BARTER P"/AU OR "BARTER P S"/AU)
              E RYE K/AU
L113          3 SEA ABB=ON  PLU=ON  "RYE K"/AU
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                E WATTENBERG B/AU
L114          4 SEA ABB=ON  PLU=ON  ("WATTENBERG B"/AU OR "WATTENBERG B W"/AU)
                E PITSON S/AU
L115          7 SEA ABB=ON  PLU=ON  ("PITSON S"/AU OR "PITSON S M"/AU)
L116         43 SEA ABB=ON  PLU=ON  L106 AND (L108 OR L109 OR L110 OR L111 OR
                L112 OR L113 OR L114 OR L115)
L117          0 SEA ABB=ON  PLU=ON  L106 AND (L109 OR L110 OR L111 OR L112 OR
                L113 OR L114 OR L115)
L118        219 SEA ABB=ON  PLU=ON  L106 AND (L96 OR L97 OR L99 OR L100 OR
                L101)
L119        206 SEA ABB=ON  PLU=ON  L118 AND L107
L120         67 SEA ABB=ON  PLU=ON  L119 NOT (PY>1998 OR AY>1998 OR PRY>1998)
L121         32 SEA ABB=ON  PLU=ON  L120 AND US/PC
L122         21 SEA ABB=ON  PLU=ON  (1982-06761J/AN OR 1982-18203E/AN OR
                1982-97729E/AN OR 1985-012102/AN OR 1985-100540/AN OR 1985-2511
                19/AN OR 1986-112662/AN OR 1986-225518/AN OR 1986-299670/AN OR
                1987-300662/AN OR 1987-322625/AN OR 1987-349712/AN OR 1988-0211
                84/AN OR 1989-078470/AN OR 1989-093242/AN OR 1989-116266/AN OR
                1989-284608/AN OR 1990-024316/AN OR 1992-006838/AN OR 1992-2999
                69/AN OR 1994-263279/AN) AND L121
L123          8 SEA ABB=ON  PLU=ON  (1982-18203E/AN OR 1985-012102/AN OR
                1986-112662/AN OR 1986-225518/AN OR 1987-349712/AN OR 1989-0932
                42/AN OR 1989-284608/AN OR 1992-006838/AN) AND L122
                D QUE L81
L124         86 SEA ABB=ON  PLU=ON  ((ATP OR ADENOSINE (2A)(TETRAHYDROGEN OR
                TETRA (1A)HYDROGEN) (1A)(TRIPHOSPHATE OR TRI(1A)PHOSPHATE))(1A)
                33P)/BIX
                E ATP/DRN
                E ATP/CN
                E ADENOSINE TRIPHOSPHATE/CN
L125         18 SEA ABB=ON  PLU=ON  L124 AND (L102 OR L103 OR L104 OR L105)
L126          3 SEA ABB=ON  PLU=ON  L125 AND (L108 OR L109 OR L110 OR L111 OR
                L112 OR L113 OR L114 OR L115)
L127         15 SEA ABB=ON  PLU=ON  L125 NOT L126
L128          0 SEA ABB=ON  PLU=ON  L127 AND (L96 OR L97 OR L99 OR L100 OR
                L101)
L129          0 SEA ABB=ON  PLU=ON  L127 AND L98
L130        566 SEA ABB=ON  PLU=ON  (L96 OR L97 OR L99 OR L100 OR L101) AND
                (L102 OR L103 OR L104 OR L105)
L131        103 SEA ABB=ON  PLU=ON  L130 AND R63#/M0,M1,M2,M3,M4,M5,M6
L132          7 SEA ABB=ON  PLU=ON  L131 AND (L108 OR L109 OR L110 OR L111 OR
                L112 OR L113 OR L114 OR L115)
L133         10 SEA ABB=ON  PLU=ON  L126 OR L132
L134         96 SEA ABB=ON  PLU=ON  L131 NOT L133
L135         92 SEA ABB=ON  PLU=ON  L134 AND L107
L136          4 SEA ABB=ON  PLU=ON  L135 NOT (PY>1998 OR AY>1998 OR PRY>1998)

=> b hcap
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FILE COVERS 1907 - 23 Jun 2005  VOL 142 ISS 26
FILE LAST UPDATED: 22 Jun 2005  (20050622/ED)
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 substance identification.

=> d all l94 tot

L94  ANSWER 1 OF 3  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2005:36538  HCAPLUS
DN   142:107384
ED   Entered STN:  14 Jan 2005
TI   Method of modulating cell growth by modulating sphingosine
     kinase for treatment of cancer and useful agents
IN   Vadas, Mathew; Gamble, Jennifer; Xia, Pu;
     Wang, Lijun; Sukocheva, Olga
PA   Medvet Science Pty Ltd., Australia
SO   U.S. Pat. Appl. Publ., 35 pp., Cont.-in-part of U.S. Ser. No. 275,686.
     CODEN: USXXCO
DT   Patent
LA   English
IC   ICM  A61K038-17
INCL 514002000
CC   1-6 (Pharmacology)
     Section cross-reference(s): 14
FAN.CNT 2
     PATENT NO.          KIND  DATE        APPLICATION NO.         DATE
     ---------------     ----  --------    --------------------    --------
PI   US 2005009732        A1   20050113    US 2004-780897          20040219
     US 2004014635        A1   20040122    US 2003-275686          20030625
PRAI AU 2003-900729       A    20030219
     US 2003-447707P      P    20030219
     US 2003-275686       A2   20030625
     AU 2000-7447         A    20000511
     WO 2001-AU539        W    20010511
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
 --------------  -----  ----------------------------------------------
 US 2005009732   ICM    A61K038-17
                 INCL   514002000
 US 2005009732   NCL    514/002.000
 US 2004014635   NCL    514/001.000
                 ECLA   A61K031/13; C12N009/12B1
AB   A method of modulating the growth of a cell, such as a neoplastic or
     malignant cell from the colon, stomach, lung, brain, bone, esophagus,
     pancreas, breast, ovary or uterus includes contacting the cell with an
     agent for a time and under conditions sufficient to modulate the
     functional activity of sphingosine kinase in which
     down-regulation of the functional activity of the sphingosine
     kinase down-regulates growth of the cells and up-regulation of the
     functional activity of this sphingosine kinase up-regulates the
     growth of the cell.  The down-regulation can reduce the functional
     activity of this sphingosine kinase to an oncogenic ineffective
     level.  Agents useful in the invention include N,N-dimethylspingosine and
     DL-threo-dihydrosphingosine.  A correlation between cell growth,
     in particular oncogenesis, and modulation in the level of activity of
     sphingosine kinase was determined for 3T3 fibroblasts and for MCF-7
     breast cancer cells.  Mice injected with 3T3 cells overexpressing
     sphingosine kinase developed tumors within 3 to 4 wk.
ST   cell growth modulation sphingosine kinase; antitumor
     sphingosine kinase down regulation cell growth; tumorigenesis
     sphingosine kinase overexpression
IT   Biological materials
        (anal. of; modulating cell growth by modulating sphingosine
        kinase for treatment of cancer and useful agents)
IT   Nucleic acid hybridization
```

(assay for **sphingosine** kinase for diagnosis; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Intestine, neoplasm
(colon; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Nucleic acids
RL: **ANT (Analyte)**; BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(for **sphingosine** kinase, screening for, for diagnosis; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT cDNA
RL: ADV (Adverse effect, including toxicity); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(for **sphingosine** kinase; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Cell proliferation
(inhibition; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Antitumor agents
Bone, neoplasm
Brain, neoplasm
Cell
Cell proliferation
Drug delivery systems
Esophagus, neoplasm
Human
Lung, neoplasm
Mammalia
Mammary gland, neoplasm
Neoplasm
Ovary, neoplasm
Pancreas, neoplasm
Prophylaxis
Second messenger system
Signal transduction, biological
Stomach, neoplasm
Uterus, neoplasm
(modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Diagnosis
(of unwanted cell growth; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(oncogene; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Gene, animal
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(ras; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Neoplasm
(solid; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT Transformation, neoplastic
(**sphingosine** kinase in; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT 50-28-2, Estra-1,3,5(10)-triene-3,17-diol (17β)-, biological studies
RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(effect of **sphingosine** kinase on transformation of MCF-7

cells promoted by; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT 119567-63-4, N,N-**Dimethylsphingosine**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT 287713-61-5, GenBank AF200328
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT 50864-48-7P, **Sphingosine** kinase
RL: ADV (Adverse effect, including toxicity); **ANT (Analyte)**; BPN (Biosynthetic preparation); BSU (Biological study, unclassified); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(modulators; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

IT 137632-07-6, Erk1 kinase 137632-08-7, Erk2 kinase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(**sphingosine** kinase in E2-dependent activation of; modulating cell growth by modulating **sphingosine** kinase for treatment of cancer and useful agents)

L94 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:561691 HCAPLUS
DN 141:238669
ED Entered STN: 14 Jul 2004
TI An assay for **sphingosine** kinase activity using biotinylated **sphingosine** and streptavidin-coated membranes
AU Roberts, Jane L.; Moretti, Paul A. B.; Darrow, Andrew L.; Derian, Claudia K.; **Vadas, Mathew A.**; **Pitson, Stuart M.**
CS Division of Human Immunology, Hanson Institute, Institute of Medical and Veterinary Science, Adelaide, 5000, Australia
SO Analytical Biochemistry (2004), 331(1), 122-129
CODEN: ANBCA2; ISSN: 0003-2697
PB Elsevier Science
DT Journal
LA English
CC 7-1 (Enzymes)

AB **Sphingosine** kinase catalyzes the phosphorylation of **sphingosine** to generate **sphingosine** 1-phosphate, a lipid signaling mol. implicated in roles in a diverse range of mammalian cell processes through its action as both a ligand for G-protein-coupled cell-surface receptors and an apparent intracellular second messenger. This paper describes a rapid, sensitive, and reproducible assay for **sphingosine** kinase activity using biotinylated **sphingosine** (biotinyl-Sph) as a substrate and capturing the phosphorylated product with streptavidin-coated membranes. We have shown that both human **sphingosine** kinase 1 and 2 (hSK1 and hSK2) can efficiently phosphorylate biotinyl-Sph, with Km values similar to those of **sphingosine.** The assay utilizing this substrate has high sensitivity for hSK1 and hSK2, with detection limits in the low-femtomole range for both purified recombinant enzymes. Importantly, we have also demonstrated the capacity of this assay to measure endogenous **sphingosine** kinase activity in crude cell exts. and to follow changes in this activity following **sphingosine** kinase activation. Together, these results demonstrate the potential utility of this assay in both cell-based anal. of **sphingosine** kinase signaling pathways and high-throughput screens for agents affecting **sphingosine** kinase activity in vitro.

ST **sphingosine** kinase detn biotinylated **sphingosine** streptavidin coated membrane

IT Michaelis constant
Phosphorylation, biological

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     Signal transduction, biological
        (assay for sphingosine kinase activity using biotinylated
        sphingosine and streptavidin-coated membranes)
IT   Human
        (sphingosine kinases 1 and 2; assay for sphingosine
        kinase activity using biotinylated sphingosine and
        streptavidin-coated membranes)
IT   Membranes, nonbiological
        (streptavidin-coated; assay for sphingosine kinase activity
        using biotinylated sphingosine and streptavidin-coated
        membranes)
IT   50864-48-7, Sphingosine kinase
     RL: ANT (Analyte); BSU (Biological study, unclassified); ANST
     (Analytical study); BIOL (Biological study)
        (1 and 2; assay for sphingosine kinase activity using
        biotinylated sphingosine and streptavidin-coated membranes)
IT   2964-07-0   9013-20-1, Streptavidin   752987-57-8
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (assay for sphingosine kinase activity using biotinylated
        sphingosine and streptavidin-coated membranes)
RE.CNT  31    THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(3) Buehrer, B; J Biol Chem 1992, V267, P3154 HCAPLUS
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L94  ANSWER 3 OF 3  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1999:193987  HCAPLUS
DN   130:232524
ED   Entered STN:  25 Mar 1999
TI   A method of modulating cellular activity
IN   Vadas, Mathew; Gamble, Jennifer; Xia, Pu;
     Barter, Philip; Rye, Kerry-Anne; Wattenberg,
     Brian; Pitson, Stuart
PA   Medvet Science Pty. Ltd., Australia
SO   PCT Int. Appl., 62 pp.
     CODEN: PIXXD2
DT   Patent
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LA   English
IC   ICM  A61K031-13
     ICS  A61K035-14; A61K038-00
CC   1-12 (Pharmacology)
FAN.CNT 1
     PATENT NO.          KIND  DATE        APPLICATION NO.       DATE
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PI   WO 9912533          A1    19990318    WO 1998-AU730         19980908
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
             FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI,
             CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     CA 2302838          AA    19990318    CA 1998-2302838       19980908
     AU 9889658          A1    19990329    AU 1998-89658         19980908
     AU 757358           B2    20030220
     EP 1011654          A1    20000628    EP 1998-941157        19980908
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 2001515857       T2    20010925    JP 2000-510431        19980908
     US 2002051777       A1    20020502    US 2001-977217        20011016
     US 6649362          B2    20031118
     US 2005074830       A1    20050407    US 2003-679485        20031007
PRAI AU 1997-9002        A     19970908
     WO 1998-AU730       W     19980908
     US 2000-508249      A1    20000601
     US 2001-977217      A3    20011016
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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 WO 9912533      ICM    A61K031-13
                 ICS    A61K035-14; A61K038-00
 WO 9912533      ECLA   A61K031/66D10; A61K038/17A2; A61K038/45; A61K038/45+M;
                        C12Q001/34; G01N033/53F
 US 2002051777   NCL    435/015.000; 424/094.500; 435/069.200
                 ECLA   A61K031/66D10; A61K038/17A2; A61K038/45; A61K038/45+M;
                        C12Q001/34; G01N033/53F
 US 2005074830   NCL    435/015.000; 435/021.000
                 ECLA   A61K031/66D10; A61K038/17A2; A61K038/45; A61K038/45+M;
                        C12Q001/34; G01N033/53F
AB   The present invention relates generally to a method of modulating cellular
     activity and agents useful for same.  More particularly, the present
     invention contemplates a method of modulating endothelial cell activity
     and even more particularly endothelial cell adhesion mol. expression.
     Most particularly, the present invention provides a method of treating
     conditions involving inflammatory mechanisms such as coronary heart
     disease by preventing or reducing endothelial cell adhesion mol.
     expression.  One aspect of the invention is administration of an agent
     which modulates one or more components of the sphingosine kinase
     signaling pathway (such as sphingosine kinase or
     sphingosine-1-phosphate).  The inhibitory effect of high-d.
     lipoproteins (HDL) on the sphingosine kinase signaling pathway
     was determined  A further aspect of the invention is a method for detecting
     sphingosine kinase activity using 33P-ATP and
     sphingosine in the presence of a scintillant.
ST   endothelial cell adhesion mol expression inhibition; sphingosine
     kinase signaling pathway inhibition; coronary heart disease adhesion mol
     modulation
IT   Selectins
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (E-; cellular activity response to modulating endothelial cell adhesion
        mol. expression and sphingosine kinase signaling pathway
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          using agents such as HDL in relation to treatment of inflammatory
          conditions such as coronary heart disease)
IT     Transcription factors
       RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
       (Biological study); PROC (Process)
          (NF-κB (nuclear factor κB); cellular activity response to
          modulating endothelial cell adhesion mol. expression and
          sphingosine kinase signaling pathway using agents such as HDL
          in relation to treatment of inflammatory conditions such as coronary
          heart disease)
IT     Cell adhesion molecules
       RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
       (Biological study); PROC (Process)
          (PECAM-1; cellular activity response to modulating endothelial cell
          adhesion mol. expression and sphingosine kinase signaling
          pathway using agents such as HDL in relation to treatment of
          inflammatory conditions such as coronary heart disease)
IT     Cell adhesion molecules
       RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
       (Biological study); PROC (Process)
          (VCAM-1; cellular activity response to modulating endothelial cell
          adhesion mol. expression and sphingosine kinase signaling
          pathway using agents such as HDL in relation to treatment of
          inflammatory conditions such as coronary heart disease)
IT     Anti-inflammatory agents
       Signal transduction, biological
          (cellular activity response to modulating endothelial cell adhesion
          mol. expression and sphingosine kinase signaling pathway
          using agents such as HDL in relation to treatment of inflammatory
          conditions such as coronary heart disease)
IT     Cell adhesion molecules
       RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
       (Biological study); PROC (Process)
          (cellular activity response to modulating endothelial cell adhesion
          mol. expression and sphingosine kinase signaling pathway
          using agents such as HDL in relation to treatment of inflammatory
          conditions such as coronary heart disease)
IT     Artery, disease
          (coronary; cellular activity response to modulating endothelial cell
          adhesion mol. expression and sphingosine kinase signaling
          pathway using agents such as HDL in relation to treatment of
          inflammatory conditions such as coronary heart disease)
IT     Blood vessel
          (endothelium; cellular activity response to modulating endothelial cell
          adhesion mol. expression and sphingosine kinase signaling
          pathway using agents such as HDL in relation to treatment of
          inflammatory conditions such as coronary heart disease)
IT     Ceramides
       RL: BPR (Biological process); BSU (Biological study, unclassified); MFM
       (Metabolic formation); BIOL (Biological study); FORM (Formation,
       nonpreparative); PROC (Process)
          (formation; cellular activity response to modulating endothelial cell
          adhesion mol. expression and sphingosine kinase signaling
          pathway using agents such as HDL in relation to treatment of
          inflammatory conditions)
IT     Lipoproteins
       RL: BAC (Biological activity or effector, except adverse); BSU (Biological
       study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
       (Uses)
          (high-d., 3; cellular activity response to modulating endothelial cell
          adhesion mol. expression and sphingosine kinase signaling
          pathway using agents such as HDL in relation to treatment of
          inflammatory conditions such as coronary heart disease)
IT     Sphingomyelins
       RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
       (Biological study); PROC (Process)
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          (hydrolysis; cellular activity response to modulating endothelial cell
          adhesion mol. expression and sphingosine kinase signaling
          pathway using agents such as HDL in relation to treatment of
          inflammatory conditions)
IT     Scintillation
          (in sphingosine kinase determination; cellular activity response to
          modulating endothelial cell adhesion mol. expression and
          sphingosine kinase signaling pathway using agents such as HDL)
IT     50864-48-7, Sphingosine kinase
       RL: ANT (Analyte); BPR (Biological process); BSU (Biological
       study, unclassified); ANST (Analytical study); BIOL (Biological study);
       PROC (Process)
          (cellular activity response to modulating endothelial cell adhesion
          mol. expression and sphingosine kinase signaling pathway
          using agents such as HDL in relation to treatment of inflammatory
          conditions such as coronary heart disease)
IT     119567-63-4, N,N-Dimethylsphingosine
       RL: BAC (Biological activity or effector, except adverse); BSU (Biological
       study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
       (Uses)
          (cellular activity response to modulating endothelial cell adhesion
          mol. expression and sphingosine kinase signaling pathway
          using agents such as HDL in relation to treatment of inflammatory
          conditions such as coronary heart disease)
IT     26993-30-6, Sphingosine-1-phosphate   142243-02-5, ERK kinase
       RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
       (Biological study); PROC (Process)
          (cellular activity response to modulating endothelial cell adhesion
          mol. expression and sphingosine kinase signaling pathway
          using agents such as HDL in relation to treatment of inflammatory
          conditions such as coronary heart disease)
IT     133587-41-4
       RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
          (in sphingosine kinase determination; cellular activity response to
          modulating endothelial cell adhesion mol. expression and
          sphingosine kinase signaling pathway using agents such as HDL)
RE.CNT  9      THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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(8) The Regents Of The University Of California; WO 9620710 A 1996 HCAPLUS
(9) The Rogosin Institute; WO 8809345 A 1988 HCAPLUS


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L95    ANSWER 1 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN     2002:241288  HCAPLUS
DN     136:275646
ED     Entered STN:  28 Mar 2002
TI     Method and apparatus for detecting cancerous cells using molecules that
       change electrophoretic mobility
IN     Allbritton, Nancy; Sims, Christopher
PA     The Regents of the University of California, USA
SO     U.S. Pat. Appl. Publ., 29 pp., Cont.-in-part of U.S. Ser. No. 358,504.
       CODEN: USXXCO
DT     Patent
LA     English
IC     ICM  G01N033-574
INCL 435007230
CC     9-1 (Biochemical Methods)
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     Section cross-reference(s): 7, 14
FAN.CNT 6
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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PI   US 2002037542        A1    20020328    US 2001-859650         20010517 <--
     US 6740497           B2    20040525
     US 6156576           A     20001205    US 1998-36706          19980306 <--
     US 6335201           B1    20020101    US 1999-358504         19990721 <--
     WO 2002092199        A1    20021121    WO 2002-US14755        20020509
     WO 2002092199        C1    20021227
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
             PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
             UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
             CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
             BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     EP 1392417           A1    20040303    EP 2002-769700         20020509
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
     JP 2004536586        T2    20041209    JP 2002-589115         20020509
     US 2004161807        A1    20040819    US 2004-779917         20040217 <--
PRAI US 1998-36706        A2    19980306  <--
     US 1999-358504       A2    19990721
     US 2001-859650       A     20010517
     WO 2002-US14755      W     20020509
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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 US 2002037542   ICM    G01N033-574
                 INCL   435007230
 US 2002037542   NCL    435/015.000; 435/029.000
                 ECLA   C12Q001/00; C12Q001/48B; G01N033/50; G01N033/50D2D2 <--
 US 6156576      NCL    436/063.000; 204/451.000; 204/452.000; 204/453.000;
                        204/601.000; 204/603.000; 204/604.000; 422/082.050;
                        422/082.080; 435/004.000; 435/029.000; 435/288.700;
                        436/164.000; 436/172.000
                 ECLA   G01N027/447B4; G01N033/483B                         <--
 US 6335201      NCL    436/063.000; 204/400.000; 204/451.000; 204/601.000;
                        422/082.050; 422/082.080; 435/004.000; 435/029.000;
                        435/030.000; 435/288.700; 436/164.000; 436/172.000
                 ECLA   G01N033/483B                                        <--
 WO 2002092199   ECLA   B01D053/62; C12Q001/48B; G01N033/50D2D2
 JP 2004536586   FTERM  4B029/AA07; 4B029/AA09; 4B029/AA27; 4B029/BB11;
                        4B029/BB16; 4B029/CC01; 4B029/FA13; 4B029/HA05;
                        4B029/HA09; 4B063/QA01; 4B063/QA20; 4B063/QQ08;
                        4B063/QQ27; 4B063/QQ79; 4B063/QR41; 4B063/QR48;
                        4B063/QR57; 4B063/QR66; 4B063/QS16; 4B063/QS28;
                        4B063/QS36; 4B063/QX01; 4B063/QX04; 4B063/QX07;
                        4D054/FA06; 4D054/FB20
 US 2004161807   NCL    435/007.230
                 ECLA   B01D053/62; C12Q001/00; C12Q001/48B; G01N027/447B4;
                        G01N033/483B; G01N033/50; G01N033/50D2D2            <--
AB   The activity of oncogenic intracellular chemical reactions of mols. is
     measured by the use of fluorescently labeled substrate mols. that undergo
     a change in electrophoretic mobility upon a chemical reaction such as that
     catalyzed by an enzyme or kinase.  Specificity is achieved by using
     labeled substrate mols. that can be acted upon only by specific oncogenic
     enzymes.  Thus the activity of an oncogenic enzyme or class of oncogenic
     enzymes can be determined  Measurements are made with the intracellular
     presence of such substrate mols., at some time of interest.  To ensure
     accuracy, measurements must be made in a timely manner so as to minimize
     chemical reactions occurring subsequent to the time of interest.  Fast
     controllable laser lysis is used to obtain the contents of said cell or
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cells into which reporter substrate mols. have been introduced. The cell contents are then subjected to capillary electrophoresis and oncogenic enzymic activity is determined by comparing amts. of unaltered substrate mols. to the amts. of altered substrate mols. which are separated by the electrophoresis and identified by the presence of a fluorescent label.

ST app detecting cancer cell enzyme capillary electrophoresis; kinase cancer fluorescent substrate capillary electrophoresis

IT Animal cell line
(3T3; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Capillary electrophoresis
(PERT-CE (piezoelec. sampling/rapid translation/capillary electrophoresis); method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Animal cell line
(RBL-2H3; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Fluorescent substances
(as label; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT **Isotopes**
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(as labels; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Carbohydrates, reactions
Nucleic acids
Organic compounds, reactions
Peptides, reactions
Phospholipids, reactions
Polymers, reactions
Polysaccharides, reactions
Proteins
RL: ARG (Analytical reagent use); **RCT (Reactant)**; ANST (Analytical study); **RACT (Reactant or reagent)**; USES (Uses)
(as substrates; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Analytical apparatus
(biochem.; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Enzymes, **analysis**
RL: **ANT (Analyte)**; CAT (Catalyst use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(cancer-related; method and **apparatus** for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Diagnosis
Diagnosis
(cancer; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Sampling apparatus
(cell; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Polymers, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(conjugates, with fluorescent labels, as substrates; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Peptides, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(conjugates, with fluorescent substances, as substrates; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

IT Apparatus
(fast controlled cell lysis; method and apparatus for detecting cancerous cells using mols. that change electrophoretic mobility)

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IT   ESR (electron spin resonance)
        (labels; method and apparatus for detecting cancerous cells using mols. that
        change electrophoretic mobility)
IT   Analytical apparatus
     Bioassay
     Capillary electrophoresis
     Capillary tubes
     Computers
     Cytolysis
     Data processing
     ESR spectroscopy
     Electrophoresis
     Electroporation
     Fluorometry
     Fusion, biological
     Laser fluorometry
     Mass spectrometry
     Micellar electrokinetic capillary chromatography
     Photomultipliers
     Piezoelectric apparatus
     Sensors
     Voltammetry
        (method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   Injectors
        (microinjectors, in introducing substrate into cell; method and apparatus
        for detecting cancerous cells using mols. that change electrophoretic
        mobility)
IT   Egg
        (oocyte, Xenopus laevis; method and apparatus for detecting cancerous cells
        using mols. that change electrophoretic mobility)
IT   Xenopus laevis
        (oocytes; method and apparatus for detecting cancerous cells using mols.
        that change electrophoretic mobility)
IT   Organelle
        (pinosome, pinocytic loading, in introducing substrate into cell;
        method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   Phosphorylation, biological
        (protein; method and apparatus for detecting cancerous cells using mols.
        that change electrophoretic mobility)
IT   Liposomes
        (vesicle fusion, in introducing substrate into cell; method and apparatus
        for detecting cancerous cells using mols. that change electrophoretic
        mobility)
IT   Fusion, biological
        (with vesicle, in introducing substrate into cell; method and apparatus for
        detecting cancerous cells using mols. that change electrophoretic
        mobility)
IT   405519-71-3P
     RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);
     PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); ANST
     (Analytical study); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (as cdc2 kinase substrate; method and apparatus for detecting cancerous
        cells using mols. that change electrophoretic mobility)
IT   405095-29-6P
     RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);
     PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); ANST
     (Analytical study); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (as substrate for PKA; method and apparatus for detecting cancerous cells
        using mols. that change electrophoretic mobility)
IT   405095-27-4P
     RL: ARG (Analytical reagent use); BSU (Biological study, unclassified);
     PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); ANST
     (Analytical study); BIOL (Biological study); PREP (Preparation); RACT
     (Reactant or reagent); USES (Uses)
        (as substrate; method and apparatus for detecting cancerous cells using
        mols. that change electrophoretic mobility)
IT   9002-98-6, PEI
     RL: DEV (Device component use); USES (Uses)
        (capillary coated with; method and apparatus for detecting cancerous cells
        using mols. that change electrophoretic mobility)
IT   142008-29-5, Protein kinase A   143375-65-9, Cdc2 kinase
     RL: ANT (Analyte); BSU (Biological study, unclassified); CAT
     (Catalyst use); ANST (Analytical study); BIOL (Biological study); USES
     (Uses)
        (method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   141436-78-4, Protein kinase C
     RL: ANT (Analyte); CAT (Catalyst use); ANST (Analytical study);
     USES (Uses)
        (method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   9031-44-1, Kinase   138238-67-2, Bcr-abl tyrosine kinase
     RL: ANT (Analyte); CAT (Catalyst use); DGN (Diagnostic use);
     ANST (Analytical study); BIOL (Biological study); USES (Uses)
        (method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   16561-29-8, PMA   30827-99-7, Pefabloc   65528-98-5   138067-56-8, Calcium
     Orange
     RL: BUU (Biological use, unclassified); BIOL (Biological study); USES
     (Uses)
        (method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   136795-05-6DP, resin-bound
     RL: PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); PREP
     (Preparation); RACT (Reactant or reagent)
        (method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   405095-28-5P
     RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
        (method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   92557-80-7, 5-Carboxyfluorescein succinimidyl ester   117548-22-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (method and apparatus for detecting cancerous cells using mols. that change
        electrophoretic mobility)
IT   121545-65-1   149155-45-3
     RL: PRP (Properties)
        (unclaimed sequence; method and apparatus for detecting cancerous cells
        using mols. that change electrophoretic mobility)

L95  ANSWER 2 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2002:220333  HCAPLUS
DN   136:244005
ED   Entered STN:  22 Mar 2002
TI   Enzyme method for detecting sphingosine-1-phosphate (S1P)
IN   Skinner, Michael K.; Johnson, Jodi L.; Parrott, Jeff A.
PA   Atairgin Technologies, Inc., USA
SO   PCT Int. Appl., 22 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  A61K
CC   9-2 (Biochemical Methods)
     Section cross-reference(s): 7
FAN.CNT 1
     PATENT NO.          KIND   DATE       APPLICATION NO.         DATE
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PI   WO 2002022078        A2    20020321   WO 2001-US28807         20010913
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     WO 2002022078        A3    20020718
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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             GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
             LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL,
             PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG,
             UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
     US 6448023           B1    20020910    US 2000-661988         20000914
     AU 2001090946        A5    20020326    AU 2001-90946          20010913
     US 2002127628        A1    20020912    US 2002-133012         20020426
     US 6716595           B2    20040406
PRAI US 2000-661988       A     20000914
     WO 2001-US28807      W     20010913
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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 WO 2002022078   ICM    A61K
 WO 2002022078   ECLA   C12Q001/32; C12Q001/527; C12Q001/66
 US 6448023      NCL    435/008.000; 435/004.000; 435/025.000; 435/026.000;
                        435/975.000; 436/064.000
                 ECLA   C12Q001/32; C12Q001/527; C12Q001/66
 US 2002127628   NCL    435/008.000; 435/004.000; 435/968.000
                 ECLA   C12Q001/32; C12Q001/527; C12Q001/66
AB   The present invention relates to non-radioactive enzymic methods for
     detecting Sphingosine-1-Phosphate (S1P) in biol. fluids.  The present
     invention further relates to a method of detecting the presence of cancer
     in a patient by the use of these and other methods of detecting S1P in
     biol. samples from a patient.
ST   enzymic sphingosine phosphate detection body fluid; cancer enzyme
     sphingosine phosphate body fluid
IT   Blood-group substances
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (Lea, sialyl, determination of; enzyme method for detecting sphingosine
        -1-phosphate (S1P) in body fluid)
IT   Mucins
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (MUC1, determination of; enzyme method for detecting sphingosine
        -1-phosphate (S1P) in body fluid)
IT   Proteins
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (OVX1, determination of; enzyme method for detecting sphingosine
        -1-phosphate (S1P) in body fluid)
IT   Body fluid
        (anal. of; enzyme method for detecting sphingosine-1-phosphate (S1P) in
        body fluid)
IT   Analysis
     Process automation
        (automated anal.; enzyme method for detecting sphingosine-1-phosphate
        (S1P) in body fluid)
IT   Diagnosis
     Diagnosis
        (cancer; enzyme method for detecting sphingosine-1-phosphate (S1P) in
        body fluid)
IT   Mammary gland, neoplasm
     Ovary, neoplasm
     Oviduct
     Peritoneum, neoplasm
     Uterus, neoplasm
        (carcinoma, diagnosis of; enzyme method for detecting
        sphingosine-1-phosphate (S1P) in body fluid)
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IT Uterus, neoplasm
(cervix, carcinoma, diagnosis of; enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT Carcinoma
(cervix, diagnosis of; enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT CA 125 (carbohydrate antigen)
CA19-9 antigen
Carcinoembryonic antigen
Ceramides
Glycosphingolipids
Lysophosphatidic acids
Lysophosphatidylcholines
Lysophosphatidylethanolamines
Lysophosphatidylinositols
Lysophosphatidylserines
Phosphatidylcholines, analysis
Phosphatidylethanolamines, analysis
Phosphatidylinositols
Prostate-specific antigen
Sphingomyelins
Sphingosines
RL: **ANT (Analyte)**; DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(determination of; enzyme method for detecting **sphingosine** -1-phosphate (S1P) in body fluid)
IT Carcinoma
(diagnosis of; enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT Carcinoma
(endometrial, diagnosis of; enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT Uterus, neoplasm
(endometrium, carcinoma, diagnosis of; enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT Blood analysis
Diagnosis
Fluorometry
Human
Luminescence spectroscopy
Mass spectrometry
Spectrophotometry
Test kits
(enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT Phosphatidylglycerols
RL: **ANT (Analyte)**; DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(enzyme method for detecting **sphingosine**-1-phosphate (S1P) in body fluid)
IT Enzymes, biological studies
RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT Sphingolipids
RL: PUR (Purification or recovery); PREP (Preparation)
(enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT Reagents
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(inhibitors; enzyme method for detecting sphingosine-1-phosphate (S1P) in body fluid)
IT Aldehydes, biological studies
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); **RCT (Reactant)**; BIOL (Biological study); FORM (Formation,

```
     nonpreparative); RACT (Reactant or reagent)
        (long-chain; enzyme method for detecting sphingosine
        -1-phosphate (S1P) in body fluid)
IT   Lysophosphatides
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (lysophosphatidylglycerols, determination of; enzyme method for detecting
        sphingosine-1-phosphate (S1P) in body fluid)
IT   Carcinoma
        (mammary, diagnosis of; enzyme method for detecting
        sphingosine-1-phosphate (S1P) in body fluid)
IT   Solvent extraction
        (organic, in sphingolipids enrichment; enzyme method for detecting
        sphingosine-1-phosphate (S1P) in body fluid)
IT   Carcinoma
        (ovarian, diagnosis of; enzyme method for detecting
        sphingosine-1-phosphate (S1P) in body fluid)
IT   Lysophospholipids
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (total, determination of; enzyme method for detecting sphingosine
        -1-phosphate (S1P) in body fluid)
IT   Carcinoma
        (uterine, diagnosis of; enzyme method for detecting
        sphingosine-1-phosphate (S1P) in body fluid)
IT   Interleukin 2 receptors
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (α chain, determination of; enzyme method for detecting
        sphingosine-1-phosphate (S1P) in body fluid)
IT   Interleukin 2 receptors
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (α chain, soluble, determination of; enzyme method for detecting
        sphingosine-1-phosphate (S1P) in body fluid)
IT   9014-00-0, Bacterial luciferase
     RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (bacterial; enzyme method for detecting sphingosine-1-phosphate (S1P)
        in body fluid)
IT   57-03-4, Glycerol-3-phosphate   764-22-7, Sphinganine
     9001-84-7, Phospholipase A2   81627-83-0, Macrophage colony-stimulating
     factor
     RL: ANT (Analyte); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (determination of; enzyme method for detecting sphingosine
        -1-phosphate (S1P) in body fluid)
IT   53-57-6, NADPH   58-68-4, NADH
     RL: ANT (Analyte); DGN (Diagnostic use); FMU (Formation,
     unclassified); RCT (Reactant); ANST (Analytical study); BIOL
     (Biological study); FORM (Formation, nonpreparative); RACT (Reactant
     or reagent); USES (Uses)
        (enzyme method for detecting sphingosine-1-phosphate (S1P) in
        body fluid)
IT   26993-30-6, Sphingosine-1-phosphate
     RL: ANT (Analyte); DGN (Diagnostic use); RCT (Reactant)
     ; ANST (Analytical study); BIOL (Biological study); RACT (Reactant or
     reagent); USES (Uses)
        (enzyme method for detecting sphingosine-1-phosphate (S1P) in
        body fluid)
IT   9028-86-8, NAD-dependent aldehyde dehydrogenase   9028-87-9,
     NADP-dependent aldehyde dehydrogenase   39391-27-0, Sphingosine-1-
     phosphate lyase   64295-83-6, NAD(P)H:FMN oxidoreductase
     RL: ARG (Analytical reagent use); DGN (Diagnostic use); ANST (Analytical
     study); BIOL (Biological study); USES (Uses)
        (enzyme method for detecting sphingosine-1-phosphate (S1P) in body
     fluid)
IT   1071-23-4
     RL: BSU (Biological study, unclassified); FMU (Formation, unclassified);
     RCT (Reactant); BIOL (Biological study); FORM (Formation,
     nonpreparative); RACT (Reactant or reagent)
        (enzyme method for detecting sphingosine-1-phosphate (S1P) in
        body fluid)
IT   146-17-8, FMN
     RL: FMU (Formation, unclassified); RCT (Reactant); FORM
     (Formation, nonpreparative); RACT (Reactant or reagent)
        (enzyme method for detecting sphingosine-1-phosphate (S1P) in
        body fluid)

L95  ANSWER 3 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2000:405833  HCAPLUS
DN   133:219701
ED   Entered STN:  20 Jun 2000
TI   Quantitative Measurement of Sphingosine 1-Phosphate by
     Radioreceptor-Binding Assay
AU   Murata, Naoya; Sato, Koichi; Kon, Junko; Tomura, Hideaki; Okajima,
     Fumikazu
CS   Laboratory of Signal Transduction, Institute for Molecular and Cellular
     Regulation, Gunma University, Maebashi, 371-8512, Japan
SO   Analytical Biochemistry (2000), 282(1), 115-120
     CODEN: ANBCA2; ISSN: 0003-2697
PB   Academic Press
DT   Journal
LA   English
CC   9-8 (Biochemical Methods)
     Section cross-reference(s): 13
AB   In Chinese hamster ovary cells overexpressing Edg-1, one of the
     sphingosine 1-phosphate (S1P) receptor subtypes, [3H]S1P binding was
     displaced by unlabeled S1P with IC50, a half-maximal concentration to inhibit the
     binding, of about 20 nM.  This radioreceptor binding was used for quant.
     measurement of S1P.  Among the various lipids employed, only
     sphingosylphosphorylcholine (SPC), other than S1P, practically displaced
     the binding; however, the potency of SPC was about 100 to 1000 times less
     than that of S1P. Thus, SPC bound to the S1P receptors inefficiently.
     Furthermore, before the application of test samples to this assay, S1P was
     partially purified: the lipid was extracted first into the aqueous phase and separated
     from other lipids under alkaline conditions, and then reextd. into the
     chloroform phase under acidic conditions.  With this assay, we could
     specifically and quant. measure S1P from 2 to 40 pmol per assay well in
     biol. samples including serum samples and various tissues.  This assay
     also allowed us to measure the change in cellular S1P content in U937
     cells after treatment with exogenous sphingosine.  (c) 2000 Academic
     Press.
ST   sphingosine phosphate radioreceptor binding assay
IT   Animal cell line
        (CHO, overexpressing receptor Edg-1; quant. measurement of sphingosine
        1-phosphate by radioreceptor-binding assay)
IT   Animal cell line
        (U937; quant. measurement of sphingosine 1-phosphate by
        radioreceptor-binding assay)
IT   Sphingomyelins
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (carbon-14 labeled, derivs.; quant. measurement of sphingosine
        1-phosphate by radioreceptor-binding assay)
IT   Receptors
     RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BPR
     (Biological process); BSU (Biological study, unclassified); ANST
     (Analytical study); BIOL (Biological study); PREP (Preparation); PROC
     (Process); USES (Uses)
        (lysophosphatidic acid, Edg-1, for sphingosine phosphate; quant.
        measurement of sphingosine 1-phosphate by radioreceptor-binding assay)
IT   Blood analysis
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      Brain
      Heart
      Intestine
      Kidney
      Liver
      Lung
      Muscle
      Spleen
      Testis
         (quant. measurement of sphingosine 1-phosphate by radioreceptor-binding
         assay)
IT    Sphingosines
      RL: BAC (Biological activity or effector, except adverse); BSU (Biological
      study, unclassified); BIOL (Biological study)
         (quant. measurement of sphingosine 1-phosphate by radioreceptor-binding
         assay)
IT    50864-48-7, Sphingosine kinase
      RL: CAT (Catalyst use); USES (Uses)
         (in synthesis of radiolabeled sphingosine phosphate; quant. measurement
         of sphingosine 1-phosphate by radioreceptor-binding assay)
IT    26993-30-6P, Sphingosine 1-Phosphate
      RL: ANT (Analyte); BOC (Biological occurrence); BPR (Biological
      process); BSU (Biological study, unclassified); PUR (Purification or
      recovery); ANST (Analytical study); BIOL (Biological study); OCCU
      (Occurrence); PREP (Preparation); PROC (Process)
         (quant. measurement of sphingosine 1-phosphate by
         radioreceptor-binding assay)
IT    291762-72-6P
      RL: ARG (Analytical reagent use); BPR (Biological process); BSU
      (Biological study, unclassified); SPN (Synthetic preparation); ANST
      (Analytical study); BIOL (Biological study); PREP (Preparation); PROC
      (Process); USES (Uses)
         (quant. measurement of sphingosine 1-phosphate by radioreceptor-binding
         assay)
IT    1670-26-4, Sphingosylphosphorylcholine
      RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
      (Biological study); PROC (Process)
         (quant. measurement of sphingosine 1-phosphate by radioreceptor-binding
         assay)
IT    291762-74-8P
      RL: BPR (Biological process); BSU (Biological study, unclassified); SPN
      (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC
      (Process)
         (quant. measurement of sphingosine 1-phosphate by radioreceptor-binding
         assay)
IT    291762-73-7
      RL: RCT (Reactant); RACT (Reactant or reagent)
         (quant. measurement of sphingosine 1-phosphate by
         radioreceptor-binding assay)
RE.CNT  18    THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) An, S; FEBS Lett 1997, V417, P279 HCAPLUS
(2) Desai, N; J Cell Biol 1993, V121, P1385 HCAPLUS
(3) Edsall, L; Anal Biochem 1999, V272, P80 HCAPLUS
(4) Hannun, Y; Science 1987, V235, P670 HCAPLUS
(5) Hla, T; Biochem Pharmacol 1999, V58, P201 HCAPLUS
(6) Hla, T; J Biol Chem 1990, V265, P9308 HCAPLUS
(7) Igarashi, Y; J Biochem 1997, V122, P1080 HCAPLUS
(8) Kon, J; J Biol Chem 1999, V274, P23940 HCAPLUS
(9) Lee, M; Science 1998, V279, P1552 HCAPLUS
(10) Mano, N; Anal Biochem 1997, V244, P291 HCAPLUS
(11) Okamoto, H; J Biol Chem 1998, V273, P27104 HCAPLUS
(12) Spiegel, S; FASEB J 1996, V10, P1388 HCAPLUS
(13) van Brocklyn, J; J Cell Biol 1998, V142, P229 HCAPLUS
(14) van Veldhoven, P; FEBS Lett 1994, V350, P91 HCAPLUS
(15) Yatomi, Y; Anal Biochem 1995, V230, P315 HCAPLUS
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(16) Yatomi, Y; FEBS Lett 1997, V404, P173 HCAPLUS
(17) Yatomi, Y; J Biochem 1997, V121, P969 HCAPLUS
(18) Zondag, G; Biochem J 1998, V330, P605 HCAPLUS
IT   291762-73-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (quant. measurement of sphingosine 1-phosphate by
        radioreceptor-binding assay)
RN   291762-73-7  HCAPLUS
CN   4-Octadecene-1,3-diol, 2-amino-, labeled with tritium, (2S,3R,4E)- (9CI)
     (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.
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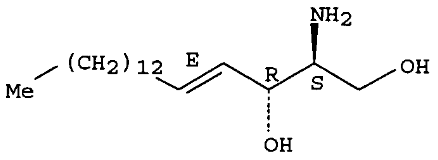

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L95  ANSWER 4 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   2000:95952  HCAPLUS
DN   132:162808
ED   Entered STN:  10 Feb 2000
TI   Fungal IPC synthase assay and methods for identifying IPC synthase
     inhibitors
IN   Radding, Jeffrey; Dickson, Robert C.; Lester, Robert L.
PA   University of Kentucky Research Foundation, USA; Eli Lilly and Company
SO   U.S., 12 pp.
     CODEN: USXXAM
DT   Patent
LA   English
IC   ICM  C12Q001-00
     ICS  C12Q001-02
INCL 435004000
CC   7-1 (Enzymes)
     Section cross-reference(s): 1, 3, 10
FAN.CNT 1
     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
     ---------------     ----   --------   --------------------   --------
PI   US 6022684           A     20000208   US 1997-944594         19971006 <--
PRAI US 1996-28079P       P     19961007  <--
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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 US 6022684      ICM    C12Q001-00
                 ICS    C12Q001-02
                 INCL   435004000
 US 6022684      NCL    435/004.000; 435/015.000; 435/029.000; 435/032.000;
                        435/035.000; 435/194.000
                 ECLA   G01N033/50D2                                  <--
AB   The presently-disclosed inositol phosphatidyl ceramide (IPC)
     synthase-inhibitor assays comprise the steps of: (1) expression of the
     IPC1 gene in a cell; (2) introducing labeled starting substrates for
     ceramide conversion as well as potential inhibitor(s) of such conversion
     to the expressed gene product in an environment which allows time and
     conditions for conversion, and (3) identifying those potential inhibitors
     which actually inhibit conversion.  The present invention also provides
     methods to determine the ability of a test compound to inhibit fungal growth,
     comprising the steps of (1) presenting active IPC synthase in a manner
     such that synthesis of inositol phosphatidyl ceramide can occur; (2)
     introducing labeled ceramide and phosphatidylinositol; (3) subjecting the
     active IPC synthase, ceramide and phosphatidylinositol to ordinary
     conditions necessary for ceramide conversion to phosphoinositol ceramide;
     and (4) identifying those test compds. which inhibit ceramide conversion
     to phosphoinositol ceramide.  A nucleotide sequence of the IPC synthase
     gene (IPC1) of S. cerevisiae AG27-61 is also disclosed.
ST   fungi inositol phosphatidyl ceramide synthase inhibitor detn;
     Saccharomyces IPC synthase gene IPC1 sequence
IT   Ceramides
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (C2-C12, labeled; fungal IPC synthase assay and methods for identifying
        IPC synthase inhibitors and nucleotide sequence of S. cerevisiae IPC1
        gene)
IT   Gene, microbial
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (IPC1; fungal IPC synthase assay and methods for identifying IPC
        synthase inhibitors and nucleotide sequence of S. cerevisiae IPC1 gene)
IT   Candida albicans
     DNA sequences
       Drug screening
     Escherichia coli
     Fluorescent indicators
     Fungicides
     Molecular cloning
     Saccharomyces
     Saccharomyces cerevisiae
     Schizosaccharomyces pombe
        (fungal IPC synthase assay and methods for identifying IPC synthase
        inhibitors and nucleotide sequence of S. cerevisiae IPC1 gene)
IT   Phosphatidylinositols
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (labeled; fungal IPC synthase assay and methods for identifying IPC
        synthase inhibitors and nucleotide sequence of S. cerevisiae IPC1 gene)
IT   Scintillation
        (scintillation proximity assay; fungal IPC synthase assay and methods
        for identifying IPC synthase inhibitors and nucleotide sequence of S.
        cerevisiae IPC1 gene)
IT   157482-45-6P, IPC synthase
     RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU
     (Biological study, unclassified); ANST (Analytical study); BIOL
     (Biological study); PREP (Preparation)
        (fungal IPC synthase assay and methods for identifying IPC synthase
        inhibitors and nucleotide sequence of S. cerevisiae IPC1 gene)
IT   86701-10-2   124753-97-5, N-Hexanoyl-sphingosine   257288-84-9
     257288-85-0   257297-58-8   257297-61-3
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (fungal IPC synthase assay and methods for identifying IPC synthase
        inhibitors and nucleotide sequence of S. cerevisiae IPC1 gene)
IT   13184-17-3P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (fungal IPC synthase assay and methods for identifying IPC synthase
        inhibitors and nucleotide sequence of S. cerevisiae IPC1 gene)
IT   258322-62-2
     RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
     (Biological study)
        (nucleotide sequence; fungal IPC synthase assay and methods for
        identifying IPC synthase inhibitors and nucleotide sequence of S.
        cerevisiae IPC1 gene)
IT   10028-17-8, Tritium, analysis 14596-37-3, Phosphorus-32,
     analysis 14762-75-5, Carbon-14, analysis
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)
        (radioactive label containing; fungal IPC synthase assay and methods for
        identifying IPC synthase inhibitors and nucleotide sequence of S.
        cerevisiae IPC1 gene)
RE.CNT  13    THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; AU 6312994 1994
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IT   10028-17-8, Tritium, analysis 14596-37-3, Phosphorus-32,
     analysis 14762-75-5, Carbon-14, analysis
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)
        (radioactive label containing; fungal IPC synthase assay and methods for
        identifying IPC synthase inhibitors and nucleotide sequence of S.
        cerevisiae IPC1 gene)
RN   10028-17-8  HCAPLUS
CN   Tritium (8CI, 9CI)  (CA INDEX NAME)


T—T

RN   14596-37-3  HCAPLUS
CN   Phosphorus, isotope of mass 32 (8CI, 9CI)  (CA INDEX NAME)


32p

RN   14762-75-5  HCAPLUS
CN   Carbon, isotope of mass 14 (8CI, 9CI)  (CA INDEX NAME)


14C


L95  ANSWER 5 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1999:565880  HCAPLUS
DN   131:181953
ED   Entered STN:  08 Sep 1999
TI   Phosphate-based dendrimers for bioassays
IN   Wilk, Andrzej; Drukier, Andrzej K.
PA   Biotraces, Inc., USA
SO   PCT Int. Appl., 53 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  A61K
CC   9-2 (Biochemical Methods)
     Section cross-reference(s): 3
FAN.CNT 1
     PATENT NO.          KIND  DATE        APPLICATION NO.        DATE
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PI   WO 9943287           A2   19990902    WO 1999-US4068         19990225 <--
     WO 9943287           A3   20000406
         W:  AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP,
             KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,
             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU,
             TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
               ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
               CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     AU 9927880          A1     19990915    AU 1999-27880         19990225 <--
PRAI US 1998-75859P      P      19980225  <--
     WO 1999-US4068      W      19990225
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
 -------------   -----  -----------------------------------------------
 WO 9943287      ICM    A61K
 WO 9943287      ECLA   C07B061/00L; C07H021/00C4; C07H021/00F; C12Q001/68B2D;
                        C12Q001/68B8; G01N033/532; G01N033/534; G01N033/58;
                        G01N033/60                                        <--
AB   A new class of bioreagents is based on "closed surface" dendrimers
     comprising a linker arm, a forking moiety and a reporter moiety that can
     conjugate to a label and to a biomol.  The bioreagents include spherical
     polymers where polymerization is controlled in order to achieve step-wise
     propagation, and thus a preselected number of reporter groups (preferably
     amines) on the surface.  Products of this step-growth are called
     generations, and the number of amine groups is doubled with each subsequent
     generation.  For the present invention the range of dendrimer generations
     is about 3-20, and the preferred range is 8-12.
ST   phosphate dendrimer bioassay
IT   Polymers, uses
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (Spherical; phosphate-based dendrimers for bioassays)
IT   Reagents
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (bio-; phosphate-based dendrimers for bioassays)
IT   Bond
        (carbon-carbon; phosphate-based dendrimers for bioassays)
IT   Glass, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (controlled pore; phosphate-based dendrimers for bioassays)
IT   Bioassay
     Biochemical molecules
     Bond
     Carboxyl group
     Carriers
     Disulfide group
     Functional groups
     Hydrolysis
     Hydroxyl group
     Immobilization, biochemical
       Immunoassay
       Isotope indicators
     Membranes, nonbiological
     Microtiter plates
     Nucleic acid hybridization
     Photolysis
     Sulfhydryl group
        (phosphate-based dendrimers for bioassays)
IT   Biopolymers
     Monosaccharides
     Oligosaccharides, analysis
     RL: ANT (Analyte); ANST (Analytical study)
        (phosphate-based dendrimers for bioassays)
IT   DNA
     RL: ANT (Analyte); ARG (Analytical reagent use); RCT (Reactant);
     ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
        (phosphate-based dendrimers for bioassays)
IT   Aldehydes, uses
     Amines, uses
     Antibodies
     Avidins
     Dendritic polymers
     Esters, uses
     Ethers, uses
     Halides
     Imides
     Polyoxyalkylenes, uses
     Probes (nucleic acid)
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (phosphate-based dendrimers for bioassays)
IT   Enzymes, uses
     RL: CAT (Catalyst use); USES (Uses)
        (phosphate-based dendrimers for bioassays)
IT   Acetals
     RL: MSC (Miscellaneous)
        (phosphate-based dendrimers for bioassays)
IT   Amino acids, miscellaneous
     RL: MSC (Miscellaneous)
        (phosphate-based dendrimers for bioassays)
IT   Peptides, miscellaneous
     RL: MSC (Miscellaneous)
        (phosphate-based dendrimers for bioassays)
IT   Sialic acids
     RL: MSC (Miscellaneous)
        (phosphate-based dendrimers for bioassays)
IT   Alkenes, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphate-based dendrimers for bioassays)
IT   Carbohydrates, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphate-based dendrimers for bioassays)
IT   Lipids, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphate-based dendrimers for bioassays)
IT   Nucleic acids
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphate-based dendrimers for bioassays)
IT   Polysaccharides, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphate-based dendrimers for bioassays)
IT   Proteins, general, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphate-based dendrimers for bioassays)
IT   Salts, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphate-based dendrimers for bioassays)
IT   Polysiloxanes, processes
     RL: REM (Removal or disposal); PROC (Process)
        (phosphate-based dendrimers for bioassays)
IT   Oligonucleotides
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (phosphate-based dendrimers for bioassays)
IT   Amino group
        (primary and secondary; phosphate-based dendrimers for bioassays)
IT   Iodination
        (radiochem.; phosphate-based dendrimers for bioassays)
IT   Functional groups
        (sulfonyl group; phosphate-based dendrimers for bioassays)
IT   58-85-5D, Biotin, conjugates   76-84-6D, ethers   9013-20-1, Streptavidin
     14158-30-6, Iodine 124, uses 14158-31-7, Iodine 125, uses
     14265-44-2, Phosphate, uses 15715-08-9, Iodine 123, uses
     17181-54-3   17655-31-1, Amide   25322-68-3   25852-91-9   34071-95-9D,
     iodo-125 derivs.
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (phosphate-based dendrimers for bioassays)
IT   9001-92-7, Protease   9031-96-3, Peptidase   9032-92-2, Glycosidase
     9075-08-5, Restriction enzyme   80498-17-5, Restriction endonuclease ecori
     81295-08-1, Restriction endonuclease msci   81295-09-2, Restriction
     endonuclease bamhi   81295-11-6, Restriction endonuclease bcli
     81295-12-7, Restriction endonuclease bglii   81295-22-9, Restriction
     endonuclease hindiii   81295-24-1, Restriction endonuclease hpai
     81295-27-4, Restriction endonuclease kpni   81295-32-1, Restriction
     endonuclease psti   81295-33-2, Restriction endonuclease pvui
     81295-34-3, Restriction endonuclease pvuii   81295-35-4, Restriction
     endonuclease saci   81295-42-3, Restriction endonuclease xbai
     81295-43-4, Restriction endonuclease Paer7I   81458-04-0, Restriction
     endonuclease mlui   82391-42-2, Restriction endonuclease smai
     83589-01-9, Restriction endonuclease clai   83589-02-0, Restriction
     endonuclease ecorv   85270-15-1, Restriction endonuclease sphi
     86352-25-2, Restriction endonuclease bstbi   86352-26-3, Restriction
     endonuclease nsii   86922-64-7, Restriction endonuclease apai
     87843-68-3, Restriction endonuclease drai   92228-44-9, Restriction
     endonuclease ncoi   92228-45-0, Restriction endonuclease nhei
     92228-46-1, Restriction endonuclease nrui   93586-00-6, Restriction
     endonuclease nari   95329-12-7, Restriction endonuclease scai
     103780-21-8, Restriction endonuclease snabi   107824-63-5   115926-60-8
     117164-98-4   124834-24-8, Restriction endonuclease Kpn2I   133876-96-7,
     Restriction endonuclease eagi
     RL: CAT (Catalyst use); USES (Uses)
        (phosphate-based dendrimers for bioassays)
IT   3483-12-3, Dithiothreitol   15056-35-6, Periodate   16984-48-8, Fluoride
     ion, reactions   20816-12-0, Osmium tetroxide
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (phosphate-based dendrimers for bioassays)
IT   14158-31-7, Iodine 125, uses 15715-08-9, Iodine 123,
     uses
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (phosphate-based dendrimers for bioassays)
RN   14158-31-7  HCAPLUS
CN   Iodine, isotope of mass 125, at. (8CI, 9CI)  (CA INDEX NAME)


125I

RN   15715-08-9  HCAPLUS
CN   Iodine, isotope of mass 123, at. (8CI, 9CI)  (CA INDEX NAME)


123I


L95  ANSWER 6 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1999:173025  HCAPLUS
DN   131:29143
ED   Entered STN:  16 Mar 1999
TI   A Scintillation Proximity Assay for the Raf/MEK/ERK Kinase Cascade:
     High-Throughput Screening and Identification of Selective Enzyme
     Inhibitors
AU   McDonald, Octerloney B.; Chen, Wen Ji; Ellis, Byron; Hoffman, Christine;
     Overton, Laurie; Rink, Martin; Smith, Albert; Marshalland, Christopher J.;
     Wood, Edgar R.
CS   Division of Biochemistry, GlaxoWellcome Inc., Research Triangle Park, NC,
     27709-13398, USA
SO   Analytical Biochemistry (1999), 268(2), 318-329
     CODEN: ANBCA2; ISSN: 0003-2697
PB   Academic Press
DT   Journal
LA   English
CC   7-1 (Enzymes)
     Section cross-reference(s): 1
AB   We have developed a quant. scintillation proximity assay (SPA) that
     reproduces the Raf/MEK/ERK signal transduction pathway.  The components of
     this assay include human cRaf1, MEK1, and ERK2 and a biotinylated peptide
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substrate for ERK2. Human cRaf1 was expressed as a his-tagged protein in insect cells in an active form. MEK1 and ERK2 were expressed in Escherichia coli as glutathione S-transferase (GST)-fusion proteins in their inactive forms. ERK2 was removed from the GST portion of the fusion protein by cleavage with thrombin protease. When the purified components are incubated together, cRaf-1 phosphorylates and activates MEK1, MEK1 phosphorylates and activates ERK2, and ERK2 phosphorylates the peptide, biotin-AAATGPLSPGPFA. Phosphorylation of the peptide using [γ-**33P]ATP** is detected following binding to streptavidin-coated SPA beads. The assay detects inhibitors of cRaf1, MEK1, or ERK2, and has been used to screen large nos. of compds. The specific target of inhibition was subsequently identified with secondary assays described herein. (c) 1999 Academic Press.

ST protein kinase cascade assay inhibitor screening; mitogen kinase cascade phosphorylation assay

IT Signal transduction, biological
(a scintillation proximity assay for the Raf/MEK/ERK kinase cascade used for high-throughput screening and selective enzyme inhibitors)

IT Phosphorylation, biological
(protein; a scintillation proximity assay for the Raf/MEK/ERK kinase cascade used for high-throughput screening and selective enzyme inhibitors)

IT 137632-07-6 137632-08-7, **Extracellular signal regulated kinase** 2 139691-76-2
RL: **ANT (Analyte)**; ANST (Analytical study)
(a scintillation proximity assay for the Raf/MEK/**ERK kinase** cascade used for high-throughput screening and selective enzyme inhibitors)

RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD

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L95  ANSWER 7 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1998:373958  HCAPLUS
DN   129:145261
ED   Entered STN:  19 Jun 1998
TI   Cellular human and viral DNA detection by nonisotopic in situ
     hybridization
AU   Herrington, C. S.
CS   Department of Pathology, Royal Liverpool University Hospital, University
     of Liverpool, UK
SO   Methods in Molecular Biology (Totowa, New Jersey) (1998),
     80(Immunochemical Protocols (2nd Edition)), 385-395
     CODEN: MMBIED; ISSN: 1064-3745
PB   Humana Press Inc.
DT   Journal
LA   English
CC   3-1 (Biochemical Genetics)
     Section cross-reference(s): 13, 14
AB   Protocols are given for the use of in situ hybridization to detect human
     papillomaviruses and repetitive genomic DNA sequences in culture cells and
     routinely processed surgical biopsies.  Procedures for preparation of slides
     for archival material, preparation of slides using CaSki cells, preparation of
     cervical smears, probe preparation and hybridization, and detection of
     biotinylated and/or digoxigenin-labeled probes.
ST   human papilloma virus DNA nonisotopic ISH; in situ hybridization human
     viral DNA
IT   Human papillomavirus
        (human papillomavirus and repetitive genomic DNA detection by
        nonisotopic in situ hybridization)
IT   Repetitive DNA
       Viral DNA
     RL: ANT (Analyte); BUU (Biological use, unclassified); THU
     (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES
     (Uses)
        (human papillomavirus and repetitive genomic DNA detection by
        nonisotopic in situ hybridization)
IT   Nucleic acid hybridization
        (in situ; human papillomavirus and repetitive genomic DNA detection by
        nonisotopic in situ hybridization)
IT   Probes (nucleic acid)
     RL: ARG (Analytical reagent use); BPN (Biosynthetic preparation); BUU
     (Biological use, unclassified); SPN (Synthetic preparation); THU
     (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (nonisotopic; human papillomavirus and repetitive genomic DNA detection
        by nonisotopic in situ hybridization)
IT   58-85-5D, Biotin, cDNA probes labeled with 1672-46-4D,
     Digoxigenin, cDNA probes labeled with
     RL: ARG (Analytical reagent use); BUU (Biological use, unclassified);
     RCT (Reactant); THU (Therapeutic use); ANST (Analytical study);
     BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
        (human papillomavirus and repetitive genomic DNA detection by
        nonisotopic in situ hybridization)
RE.CNT  14    THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
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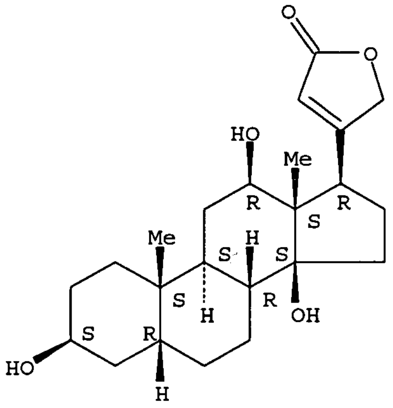
IT **1672-46-4D**, Digoxigenin, cDNA probes labeled with
RL: ARG (Analytical reagent use); BUU (Biological use, unclassified); **RCT (Reactant)**; THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); **RACT (Reactant or reagent)**; USES (Uses)
(human papillomavirus and repetitive genomic DNA detection by nonisotopic in situ hybridization)

RN 1672-46-4 HCAPLUS

CN Card-20(22)-enolide, 3,12,14-trihydroxy-, (3β,5β,12β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L95 ANSWER 8 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN

AN **1998:269349** HCAPLUS

DN 128:280452

ED Entered STN: 13 May 1998

TI Terbium Chelate Membrane Label for Time-Resolved, Total Internal Reflection Fluorescence Microscopy of Substrate-Adherent Cells

AU Phimphivong, Sam; Saavedra, S. Scott

CS Department of Chemistry, University of Arizona, Tucson, AZ, 85721, USA

SO Bioconjugate Chemistry **(1998)**, 9(3), 350-357
CODEN: BCCHES; ISSN: 1043-1802

PB American Chemical Society

DT Journal

LA English

CC 9-4 (Biochemical Methods)

AB A chelating agent conjugated to a lipid was synthesized by reacting the dianhydride form of diethylenetriaminepentaacetic acid sequentially with

4-aminosalicylate and dioleoylphosphatidylethanolamine. The product, DOPE-YAS-Tb, exhibits photophys. properties characteristic of a chelated Tb3+ ion bound to an organic triplet donor: an excitation maximum at 310 nm, narrow emission bands at 490, 545, 590, and 625 nm, and a lifetime of 1.57 ms. The suitability of DOPE-YAS-Tb as a membrane-staining agent for morphol. studies of cultured cells using total internal reflection fluorescence microscopy (TIRFM) was investigated. Swiss albino mouse 3T3 cells were cultured on silica and polystyrene substrates. Time-resolved detection was employed to reject short-lived background emission (autoemission from the cells and/or the polymer substrate), which allowed the long-lived Tb3+ emission to be selectively imaged. The results show that time-resolved TIRFM of cells stained with DOPE-YAS-Tb is an effective method of quant. examining the cell morphol. in situations where background due to autoemission from cells and/or the substrate material is problematic.

ST terbium chelate membrane label; time resolved reflection fluorescence microscopy; substrate adherent cell

IT Fluorescence microscopy
RL: **ANT (Analyte)**; ANST (Analytical study)
(Time-Resolved, Total Internal Reflection; terbium chelate membrane **label** for time-resolved, total internal reflection fluorescence microscopy of substrate-adherent cells)

IT Cell morphology
Membrane, biological
Staining, biological
(terbium chelate membrane label for time-resolved, total internal reflection fluorescence microscopy of substrate-adherent cells)

IT 205747-92-8P
RL: NUU (Other use, unclassified); SPN (Synthetic preparation); PREP (Preparation); USES (Uses)
(terbium chelate membrane label for time-resolved, total internal reflection fluorescence microscopy of substrate-adherent cells)

IT 2374-03-0 **2462-63-7** 23911-26-4
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(terbium chelate membrane label for time-resolved, total internal reflection fluorescence microscopy of substrate-adherent cells)

IT 205747-90-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(terbium chelate membrane label for time-resolved, total internal reflection fluorescence microscopy of substrate-adherent cells)

IT 205747-91-7P
RL: SPN (Synthetic preparation); PREP (Preparation)
(terbium chelate membrane label for time-resolved, total internal reflection fluorescence microscopy of substrate-adherent cells)

RE.CNT 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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(2) Axelrod, D; J Cell Biol 1981, V89, P141 MEDLINE
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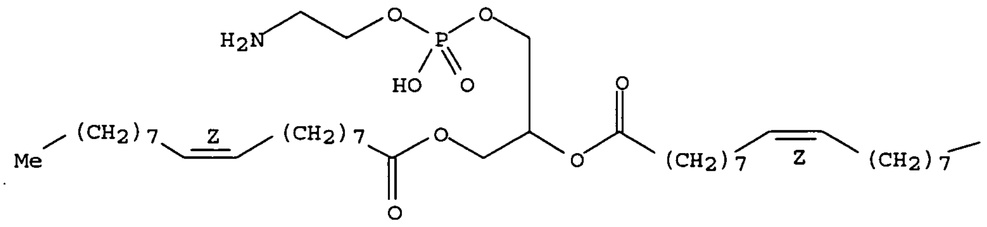
IT **2462-63-7**
RL: **RCT (Reactant); RACT (Reactant or reagent)**
(terbium chelate membrane label for time-resolved, total internal reflection fluorescence microscopy of substrate-adherent cells)
RN 2462-63-7 HCAPLUS
CN 9-Octadecenoic acid (9Z)-, 1-[[[(2-aminoethoxy)hydroxyphosphinyl]oxy]methyl]-1,2-ethanediyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

L95 ANSWER 9 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:722472 HCAPLUS
DN 128:99009
ED Entered STN: 17 Nov 1997
TI Occurrence of nonenzymic N-acetylation of sphinganine with acetyl coenzyme A producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide
AU Kashiwagi, Motoi; Mikami, Takeshi; Chiba, Masahiko; Chiba, Susumu; Matsumoto, Hiroyuki; Akino, Toyoaki; Gasa, Shinsei
CS Departments of Biochemistry, Sapporo Medical University School of Medicine, Sapporo, 060, Japan
SO Biochemistry and Molecular Biology International (1997), 42(5), 1071-1080
CODEN: BMBIES; ISSN: 1039-9712
PB Academic
DT Journal
LA English
CC 6-1 (General Biochemistry)
Section cross-reference(s): 7
AB Sphinganine, a biosynthetic precursor of ceramide, was non- enzymically acetylated with acetyl CoA at the C-2-amino residue to produce C2-H2-ceramide (N-acetyl sphinganine) in an organic solvent and in an aqueous

solution with a high yield, whereas sphingenine was only acetylated slightly. The structure of the N-acetyl sphinganine was identified with mass spectrum, and with chromatog. using an authentic N-acetylated substance. Furthermore, the C2-H2- ceramide was examined for enzymic desatn. to determine whether C2-ceramide, a cell-permeable ceramide responsible for apoptosis of cells, was produced, revealing an inferior substrate for H2-ceramide desaturase of horse brain microsomes.

ST nonenzymic acetylation sphinganine acetyl CoA ceramide; dihydroceramide desaturase acetyl sphinganine

IT Surfactants
(dihydroceramide desaturase activation; occurrence of nonenzymic N-acetylation of sphinganine with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT Brain
(dihydroceramide desaturase; occurrence of nonenzymic N-acetylation of sphinganine with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT Acetylation
(occurrence of nonenzymic N-acetylation of sphinganine with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT 7439-95-4, Magnesium, biological studies 7439-96-5, Manganese, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(dihydroceramide desaturase activation; occurrence of nonenzymic N-acetylation of sphinganine with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT 201029-35-8
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(dihydroceramide desaturase assay; occurrence of nonenzymic N-acetylation of sphinganine with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT 189398-81-0, Dihydroceramide desaturase
RL: **ANT (Analyte)**; BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(occurrence of nonenzymic N-acetylation of **sphinganine** with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT 54630-75-0
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(occurrence of nonenzymic N-acetylation of sphinganine with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT 3102-57-6 5966-29-0, N-Palmitoyl sphinganine 21830-28-4, N-Acetyl phytosphingosine 24696-26-2 26561-61-5 201029-43-8 201029-44-9
RL: BSU (Biological study, unclassified); FMU (Formation, unclassified); BIOL (Biological study); FORM (Formation, nonpreparative)
(occurrence of nonenzymic N-acetylation of sphinganine with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT 72-89-9, Acetyl CoA 554-62-1 1763-10-6, Palmitoyl CoA 2140-48-9, Butanoyl CoA **2733-29-1**, erythro-C18-**Sphingenine**
5060-32-2, n-Hexanoyl CoA
RL: BSU (Biological study, unclassified); **RCT (Reactant)**; BIOL (Biological study); **RACT (Reactant or reagent)**
(occurrence of nonenzymic N-acetylation of **sphinganine** with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

IT 13552-09-5, DL-**Sphinganine**
RL: BSU (Biological study, unclassified); **RCT (Reactant)**; BIOL

(Biological study); **RACT (Reactant or reagent)**
(DL-**Sphinganine**; occurrence of nonenzymic N-acetylation of **sphinganine** with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

RE.CNT 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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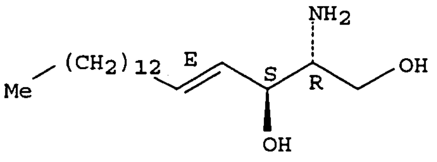
IT **2733-29-1**, erythro-C18-**Sphingenine**
RL: BSU (Biological study, unclassified); **RCT (Reactant)**; BIOL (Biological study); **RACT (Reactant or reagent)**
(occurrence of nonenzymic N-acetylation of **sphinganine** with acetyl CoA producing C2-H2-ceramide and its inconvertibility to apoptotic C2-ceramide by dihydroceramide desaturase)

RN 2733-29-1 HCAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, (2R,3S,4E)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.
Double bond geometry as shown.



L95 ANSWER 10 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:304057 HCAPLUS
DN 126:313988
ED Entered STN: 14 May 1997
TI Non-enzymic N-acetylation of sphinganine with acetyl coenzyme A
AU Kashiwagi, Motoi; Gasa, Shinsei
CS First Department of Biochemistry, Sapporo Medical University School of Medicine, Japan
SO Sapporo Igaku Zasshi (1996), 65(5), 403-414
CODEN: SIZSAR; ISSN: 0036-472X
PB Sapporo Ika Daigaku
DT Journal
LA Japanese
CC 7-3 (Enzymes)
Section cross-reference(s): 6
AB Dihydroceramide, a biosynthetic precursor of ceramide, is biol. synthesized from sphinganine and fatty acyl-CoA with acyl-CoA:sphinganine

N-acyltransferase. Interestingly, the sphinganine was found to be N-acetylated with acetyl CoA in the absence of the equine brain protein in an organic solvent or mild alkaline solution The structure of the acetylated product, that sphinganine was acetylated with at the C2-amino residue, was characterized with spectra of NMR, neg. FAB-MS, GC-MS, and GLC, as well as NaIO4-oxidation when occurring in conjunction with those of chemical synthesized, authentic N-acetylated sphinganine. The non-enzymic reactions of the sphinganine with other fatty acyl-CoAs were markedly less than those with acetyl CoA. Compared to the reaction of sphinganine with acetyl CoA, the reaction of sphingenine with acetyl CoA was not reactive, but the reaction of phytosphingosine with acetyl CoA reacted with 78.1% of the yield from the sphinganine with acetyl CoA. In contrast, the non-enzymic reaction was interfered with by added protein. These results suggest that a saturated carbon chain with free C2-amino residue in the long chain base structure could be required from the occurrence of N-acetylation, especially at C4 and C5. Non-enzymic synthesis of the N-acetyl sphinganine (dihydro-C32-ceramide) would be important in relation to apoptosis for cells. Since the dihydro-C2-ceramide might be a precursor of C2-ceramide, the possibility of the conversion was examined in the reaction of dihydroceramide desaturase in vitro. The assay for dihydroceramide desaturase was established, revealing inconvertibility and this phenomena suggests the impossibility of the generation of C2-ceramide in vivo.

ST acetylation sphinganine acetyl CoA; dihydroceramide desaturase assay ceramide

IT Acetylation
(non-enzymic N-acetylation of sphinganine with acetyl CoA)

IT 554-62-1, **Phytosphingosine**
RL: BPR (Biological process); BSU (Biological study, unclassified); **RCT (Reactant)**; BIOL (Biological study); PROC (Process); **RACT (Reactant or reagent)**
(acetyl-CoA reaction with; non-enzymic N-acetylation of **sphinganine** with acetyl CoA)

IT 189398-81-0, Dihydroceramide desaturase
RL: **ANT (Analyte)**; BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study)
(assay of; non-enzymic N-acetylation of **sphinganine** with acetyl CoA)

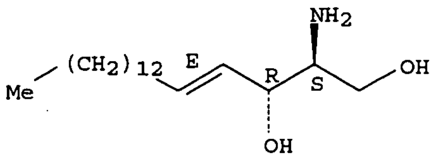
IT 13031-64-6P
RL: BPN (Biosynthetic preparation); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(non-enzymic N-acetylation of sphinganine with acetyl CoA)

IT 72-89-9, Acetyl CoA **123-78-4, Sphingenine** 764-22-7, **Sphinganine** 1763-10-6, Palmitoyl CoA
RL: BPR (Biological process); BSU (Biological study, unclassified); **RCT (Reactant)**; BIOL (Biological study); PROC (Process); **RACT (Reactant or reagent)**
(non-enzymic N-acetylation of **sphinganine** with acetyl CoA)

IT **123-78-4, Sphingenine**
RL: BPR (Biological process); BSU (Biological study, unclassified); **RCT (Reactant)**; BIOL (Biological study); PROC (Process); **RACT (Reactant or reagent)**
(non-enzymic N-acetylation of **sphinganine** with acetyl CoA)

RN 123-78-4 HCAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, (2S,3R,4E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



L95 ANSWER 11 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1997:253186 HCAPLUS
DN 126:340596
ED Entered STN: 18 Apr 1997
TI Identification of ceramides in human cells using liquid chromatography with detection by atmospheric-pressure chemical-ionization mass spectrometry
AU Couch, Letha H.; Churchwell, Mona I.; Doerge, Daniel R.; Tolleson, William H.; Howard, Paul C.
CS Division of Biochemical Toxicology, National Center for Toxicological Research, U.S. Food and Drug Administration, Jefferson, AR, 72079-9205, USA
SO Rapid Communications in Mass Spectrometry (1997), 11(5), 504-512
CODEN: RCMSEF; ISSN: 0951-4198
PB Wiley
DT Journal
LA English
CC 9-3 (Biochemical Methods)
Section cross-reference(s): 13, 14
AB Ceramides are intermediates in the biosynthesis of membrane sphingolipids. These biomols. are also important as second messengers in signal transduction pathways controlling cell growth. We developed 2 reversed-phase (RP) HPLC techniques for identification and quantification of ceramides from mammalian cells. One method was based on atmospheric-pressure chemical-ionization mass spectrometry (APCI-MS) detection of ceramides and had the advantage of requiring min. sample preparation, yielding significant structural information, and affording high sensitivity. The second method relied on perbenzoylation of the ceramides and detection at 230 nm. The predominant ceramides detected in the human leukemic HL-60 cell were N-(palmitoyl)-sphingosine, N-(nervonyl)-sphingosine, and N-(lignoceroyl)-sphingosine. When selected-ion monitoring was used with RP-HPLC/APCI-MS, approx. 2.2 pmol N-(palmitoyl)-sphingosine and 1.7 pmol N-(nervonyl)-sphingosine were observed in an extract from 40,000 HL-60 cells. Perbenzoylation with benzoyl chloride permitted RP-HPLC separation and 230-nm UV absorbance detection of the trisbenzoyl derivs. of sphingosine, N-(palmitoyl)-sphingosine, N-(nervonyl)-sphingosine, and N-(lignoceroyl)-sphingosine in the HL-60 cells. These results demonstrate the utility of utilizing two different methods coupled with APCI-MS for the quantification and identification of ceramides in biol. samples.
ST cell ceramide identification HPLC mass spectrometry; leukemia cell ceramide liq chromatog spectrometry
IT Animal cell line
(HL-60; ceramides identification in cells by HPLC with atmospheric pressure chemical-ionization mass spectrometry)
IT Chemical ionization mass spectrometry
(atmospheric-pressure; ceramides identification in cells by HPLC with atmospheric pressure chemical-ionization mass spectrometry)
IT Leukemia
Reversed phase HPLC
UV and visible spectroscopy
(ceramides identification in cells by HPLC with atmospheric pressure chemical-ionization mass spectrometry)
IT Ceramides
RL: ANT (Analyte); ANST (Analytical study)
(ceramides identification in cells by HPLC with atmospheric pressure chemical-ionization mass spectrometry)

IT Animal cell
(mammalian; ceramides identification in cells by HPLC with atmospheric
pressure chemical-ionization mass spectrometry)
IT 2304-81-6
RL: ANT (Analyte); ANST (Analytical study)
(ceramides identification in cells by HPLC with atmospheric pressure
chemical-ionization mass spectrometry)
IT 24696-26-2, N-(Palmitoyl)-**sphingosine** 34435-05-7 54164-50-0
RL: **ANT (Analyte)**; PRP (Properties); THU (Therapeutic use); ANST
(Analytical study); BIOL (Biological study); USES (Uses)
(ceramides identification in cells by HPLC with atmospheric pressure
chemical-ionization mass spectrometry)
IT 5966-29-0, N-Palmitoylsphinganine
RL: PRP (Properties)
(ceramides identification in cells by HPLC with atmospheric pressure
chemical-ionization mass spectrometry)
IT **123-78-4, Sphingosine** 764-22-7, **Sphinganine**
RL: PRP (Properties); **RCT (Reactant); RACT (Reactant or
reagent)**
(ceramides identification in cells by HPLC with atmospheric pressure
chemical-ionization mass spectrometry)
IT 992-35-8P 2304-76-9P 189811-01-6P 189811-02-7P 189811-05-0P
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(ceramides identification in cells by HPLC with atmospheric pressure
chemical-ionization mass spectrometry)
IT 98-88-4, Benzoyl chloride
RL: RCT (Reactant); RACT (Reactant or reagent)
(ceramides identification in cells by HPLC with atmospheric pressure
chemical-ionization mass spectrometry)
RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

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1996, V37, P138
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IT **123-78-4, Sphingosine**
RL: PRP (Properties); **RCT (Reactant); RACT (Reactant or
reagent)**

```
        (ceramides identification in cells by HPLC with atmospheric pressure
        chemical-ionization mass spectrometry)
RN   123-78-4  HCAPLUS
CN   4-Octadecene-1,3-diol, 2-amino-, (2S,3R,4E)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.  Rotation (-).
Double bond geometry as shown.
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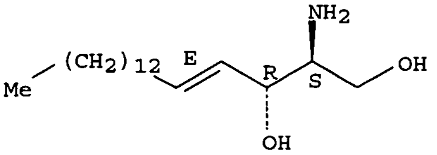

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L95  ANSWER 12 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1997:187033  HCAPLUS
DN   126:183525
ED   Entered STN:  21 Mar 1997
TI   Method for quantifying sphingosine and for diagnosing platelet activation
IN   Igarashi, Yasuyuki; Yatomi, Yutaka; Ohta, Hideki; Hakomori, Sen-itiroh
PA   Oncomembrane, Inc., USA
SO   PCT Int. Appl., 28 pp.
     CODEN: PIXXD2
DT   Patent
LA   English
IC   ICM  G01N023-00
     ICS  G01N033-92
CC   9-16 (Biochemical Methods)
     Section cross-reference(s): 13
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   WO 9701752           A1    19970116    WO 1996-US10861        19960628
         W:  CA, JP
         RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
     US 5677189           A     19971014    US 1995-496471         19950629
     CA 2222207           AA    19970116    CA 1996-2222207        19960628
     EP 835439            A1    19980415    EP 1996-922579         19960628
         R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, FI
     JP 11513110          T2    19991109    JP 1996-504030         19960628
PRAI US 1995-496471       A     19950629
     WO 1996-US10861      W     19960628
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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 WO 9701752      ICM    G01N023-00
                 ICS    G01N033-92
 WO 9701752      ECLA   G01N033/53F; G01N033/92
 US 5677189      NCL    436/057.000; 436/063.000; 436/071.000; 436/111.000
AB   The invention relates to an assay for quantifying, e.g., sphingosine and
     sphingosine 1-phosphate which can be used to ascertain platelet
     activation.  The assay for a sphingosine consists of the following steps:
     (1) extracting lipids from a biol. sample (e.g., cultured cells); (2) treating
     the extracted lipids with alkali (e.g., NaOH); (3) reacting the treated extracted
     lipids with labeled (e.g., 3H or 14C) acyl anhydride (e.g., acetic
     anhydride or propionic anhydride) to yield labeled N-acetylated lipid
     derivs.; (4) separating the labeled N-acetylated lipid derivs. by, e.g., TLC,
     into a pattern that discriminates said derivs. by label detection; and (5)
     comparing said pattern of discriminated visualized labeled derivs. with a
     known pattern of labeled sphingosine separated as in step 4.  An assay for
     determining platelet activation by quantifying sphingosine 1-phosphate in a
     biol. sample comprises performing steps 1-4 above and then comparing the
     pattern of discriminated visualized labeled derivs. with the pattern of
     labeled sphingosine 1-phosphate separated as in step 4 to identify labeled
     sphingosine 1-phosphate and then measuring the amount of labeled sphingosine
     1-phosphate.  The amount of labeled sphingosine 1-phosphate correlates pos.
     with the degree of platelet activation.
ST   sphingosine detn radioassay TLC platelet activation; platelet activation
     detection sphingosine phosphate detn; cell ext sphingosine detn radioassay
     TLC
IT   Platelet (blood)
        (activation; quantifying sphingosine and sphingosine 1-phosphate and
        diagnosing platelet activation)
IT   Cell activation
        (platelet; quantifying sphingosine and sphingosine 1-phosphate and
        diagnosing platelet activation)
IT   Animal cell
     Animal tissue culture
     TLC (thin layer chromatography)
        (quantifying sphingosine and sphingosine 1-phosphate and diagnosing
        platelet activation)
IT   Sphingosines
     RL: ANT (Analyte); ANST (Analytical study)
        (quantifying sphingosine and sphingosine
        1-phosphate and diagnosing platelet activation)
IT   123-78-4, Sphingosine   26993-30-6, Sphingosine
     1-phosphate
     RL: ANT (Analyte); ANST (Analytical study)
        (quantifying sphingosine and sphingosine
        1-phosphate and diagnosing platelet activation)
IT   108-24-7D, Acetic anhydride, labeled   123-62-6D, Propionic anhydride,
     labeled   10028-17-8D, Tritium, acyl anhydrides labeled with, reactions
     14762-75-5D, Carbon-14, acyl anhydrides labeled with, reactions
     25962-31-6, [3H]Acetic anhydride
     RL: ARG (Analytical reagent use); RCT (Reactant); ANST
     (Analytical study); RACT (Reactant or reagent); USES (Uses)
        (quantifying sphingosine and sphingosine
        1-phosphate and diagnosing platelet activation)
IT   1310-73-2, Sodium hydroxide (NaOH), analysis
     RL: ARU (Analytical role, unclassified); ANST (Analytical study)
        (quantifying sphingosine and sphingosine 1-phosphate and diagnosing
        platelet activation)

L95  ANSWER 13 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1997:85099  HCAPLUS
DN   126:86792
ED   Entered STN:  06 Feb 1997
TI   Fluorescent labeling complexes with large stokes shifts formed by coupling
     together cyanine and other fluorochromes capable of resonance energy
     transfer
IN   Waggoner, Alan Stewart; Mujumdar, Swati Ratnakar; Mujumdar, Ratnakar
     Balvant
PA   Carnegie-Mellon University, USA
SO   Eur. Pat. Appl., 29 pp.
     CODEN: EPXXDW
DT   Patent
LA   English
IC   ICM  G01N033-533
     ICS  G01N033-58; G01N033-52
CC   9-5 (Biochemical Methods)
     Section cross-reference(s): 73
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   EP 747700            A2    19961211    EP 1996-303879         19960530 <--
     EP 747700            A3    19970507
     EP 747700            B1    20011205
         R:  AT, BE, CH, DE, ES, FI, FR, GB, IT, LI, NL, SE
     US 6008373          A     19991228    US 1995-476880         19950607 <--
     GB 2301833          A1    19961218    GB 1996-11453          19960530 <--
     GB 2301833          B2    19970716
     EP 943918           A1    19990922    EP 1999-110086         19960530 <--
         R:  AT, BE, CH, DE, ES, FR, GB, IT, LI, NL, SE, FI
     AT 210292           E     20011215    AT 1996-303879         19960530 <--
     ES 2170204          T3    20020801    ES 1996-303879         19960530 <--
     CA 2178308          AA    19961208    CA 1996-2178308        19960605 <--
     JP 09104825         A2    19970422    JP 1996-146333         19960607 <--
     JP 2843296          B2    19990106
     US 6130094          A     20001010    US 1998-152009         19980911 <--
     US 6479303          B1    20021112    US 1998-151899         19980911 <--
     US 6545164          B1    20030408    US 1999-413998         19991007 <--
     US 2003220502       A1    20031127    US 2002-300459         20021120 <--
     US 6673943          B2    20040106
PRAI US 1995-476880      A     19950607  <--
     EP 1996-303879      A3    19960530  <--
     US 1999-413998      A3    19991007
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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 EP 747700       ICM    G01N033-533
                 ICS    G01N033-58; G01N033-52
 EP 747700       ECLA   G01N033/533; G01N033/58D                        <--
 US 6008373      NCL    548/427.000; 436/006.000; 544/212.000; 544/328.000;
                        546/277.400
                 ECLA   G01N033/533; G01N033/58D                        <--
 GB 2301833      ECLA   G01N033/533; G01N033/58D                        <--
 EP 943918       ECLA   G01N033/533; G01N033/58D                        <--
 US 6130094      NCL    436/063.000; 252/183.110; 252/700.000; 435/006.000;
                        435/007.100; 436/800.000; 536/022.100; 536/023.100
                 ECLA   G01N033/533; G01N033/58D                        <--
 US 6479303      NCL    436/546.000; 435/006.000; 435/007.200; 435/188.000;
                        436/527.000; 436/529.000; 436/530.000; 436/534.000;
                        436/800.000; 530/391.300; 530/391.500; 530/402.000;
                        530/409.000
                 ECLA   G01N033/533; G01N033/58D                        <--
 US 6545164      NCL    548/427.000; 435/006.000; 436/006.000; 536/023.100;
                        544/212.000; 544/328.000; 546/269.700; 546/282.700
                 ECLA   G01N033/533; G01N033/58D                        <--
 US 2003220502   NCL    548/427.000; 544/212.000; 544/328.000
                 ECLA   G01N033/533; G01N033/58D                        <--
AB   The present invention provides low-mol.-weight fluorescent labeling complexes
     with large wavelength shifts between absorption of one dye in the complex
     and emission from another dye in the complex.  These complexes can be
     used, for example, for multiparameter fluorescence cell anal. using a
     single excitation wavelength.  The low mol. weight of the complex permits
     materials labeled with the complex to penetrate cell structures for use as
     probes.  The labeling complexes are synthesized by covalently attaching
     through linkers to form donor-acceptor complexes.  Resonance energy
     transfer from an excited donor to fluorescent acceptor provides wavelength
     shifts up to 300 nm.  The fluorescent labeling complexes preferably
     contain reactive groups for the labeling of functional groups on target
     compds., such as derivatized oxy and deoxy polynucleic acids, antibodies,
     enzymes, lipids, carbohydrates, proteins, and other materials.  The
     complexes may contain functional groups permitting covalent reaction with
     materials containing reactive groups.
ST   fluorescent labeling complex prepn cell probe; biopolymer labeling
     fluorescent complex; resonance energy transfer fluorescent labeling
     complex
IT   Immunoglobulins
     RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
        (G, fluorescent-labeled; fluorescent labeling complexes with large
        Stokes shifts preparation for cell anal.)
IT   Cytometry
        (flow; fluorescent labeling complexes with large Stokes shifts preparation
```

for cell anal.)
IT Amino group
Bacteria (Eubacteria)
Biochemical molecules
Cell
Fluorescent probes
Lymphocyte
Microorganism
Mononuclear cell (leukocyte)
Pharmaceutical analysis
T cell (lymphocyte)
(fluorescent labeling complexes with large Stokes shifts preparation for cell anal.)
IT Antigens
Biopolymers
RL: **ANT (Analyte)**; ANST (Analytical study)
(fluorescent **labeling** complexes with large Stokes shifts preparation for cell anal.)
IT **DNA**
RNA
RL: **ANT (Analyte)**; ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fluorescent **labeling** complexes with large Stokes shifts preparation for cell anal.)
IT Carbonyl group
Cyanine dyes
Hydroxyl group
Phosphate group
Probes (nucleic acid)
Sulfhydryl group
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fluorescent labeling complexes with large Stokes shifts preparation for cell anal.)
IT Glass beads
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(fluorescent labeling complexes with large Stokes shifts preparation for cell anal.)
IT Polymers, analysis
RL: ARU (Analytical role, unclassified); ANST (Analytical study)
(fluorescent labeling complexes with large Stokes shifts preparation for cell anal.)
IT Antibodies
Carbohydrates, preparation
Enzymes, preparation
Lipids, preparation
Nucleic acids
Proteins, specific or class
RL: ARG (Analytical reagent use); **RCT (Reactant)**; SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); **RACT (Reactant or reagent)**; USES (Uses)
(fluorescent-labeled; fluorescent labeling complexes with large Stokes shifts preparation for cell anal.)
IT T cell (lymphocyte)
(helper cell; fluorescent labeling complexes with large Stokes shifts preparation for cell anal.)
IT 185804-13-1
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(Cascade Blue; fluorescent labeling complexes with large Stokes shifts preparation for cell anal.)
IT 2321-07-5, Fluorescein 9013-20-1D, Streptavidin, conjugates
27072-45-3, FITC 167426-61-1, Pyrenetrisulfonic acid
RL: ARG (Analytical reagent use); ANST (Analytical study); USES (Uses)
(fluorescent labeling complexes with large Stokes shifts preparation for cell anal.)
IT 185397-56-2DP, reactions products 185397-56-2P
RL: ARG (Analytical reagent use); PRP (Properties); SPN (Synthetic

```
     preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
        (fluorescent labeling complexes with large Stokes shifts preparation for
        cell anal.)
IT   146368-08-3P   185397-43-7P   185397-44-8P   185397-46-0P
     RL: ARG (Analytical reagent use); RCT (Reactant); SPN (Synthetic
     preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant
     or reagent); USES (Uses)
        (fluorescent labeling complexes with large Stokes shifts preparation for
        cell anal.)
IT   185397-41-5P   185397-42-6P   185397-47-1P   185397-48-2P   185397-49-3P
     185397-50-6P   185397-51-7P
     RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
     (Analytical study); PREP (Preparation); USES (Uses)
        (fluorescent labeling complexes with large Stokes shifts preparation for
        cell anal.)
IT   146368-10-7   146368-12-9   185397-52-8   185397-53-9   185397-54-0
     185397-55-1
     RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
        (fluorescent labeling complexes with large Stokes shifts preparation for
        cell anal.)
IT   68-12-2, reactions   108-77-0, Cyanuric chloride   118-29-6,
     N-Hydroxymethylphthalimide   1640-39-7   4224-70-8, 6-Bromohexanoic acid
     74124-79-1, Disuccinimidyl carbonate   149980-68-7   184351-56-2
     185397-38-0   185397-40-4   185397-45-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (fluorescent labeling complexes with large Stokes shifts preparation for
        cell anal.)
IT   185397-39-1P   185397-46-0DP, succinimidyl ester derivs
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (fluorescent labeling complexes with large Stokes shifts preparation for
        cell anal.)

L95  ANSWER 14 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1996:323936  HCAPLUS
DN   125:81261
ED   Entered STN:  05 Jun 1996
TI   Single-step signal group-imidazole labeling of organic phosphate groups
     under aqueous conditions
IN   Giese, Roger W.; Wang, Poguang
PA   Northeastern University, USA
SO   U.S., 9 pp.
     CODEN: USXXAM
DT   Patent
LA   English
IC   ICM  G01N033-48
INCL 436063000
CC   9-5 (Biochemical Methods)
     Section cross-reference(s): 28
FAN.CNT 1
     PATENT NO.          KIND   DATE       APPLICATION NO.        DATE
     ---------------     ----   --------   --------------------   --------
PI   US 5512486           A     19960430   US 1993-60569          19930510 <--
PRAI US 1993-60569              19930510  <--
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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 US 5512486      ICM    G01N033-48
                 INCL   436063000
 US 5512486      NCL    436/063.000; 436/094.000; 436/103.000; 436/104.000;
                        536/025.320; 548/335.100
                 ECLA   C07F005/02B; G01N033/533                         <--
OS   MARPAT 125:81261
GI
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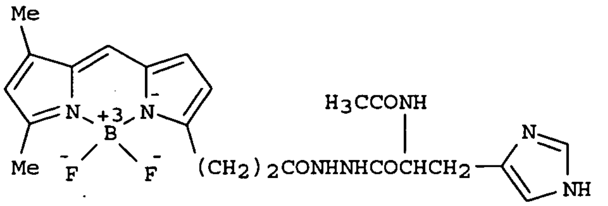


I

AB Compds. and methods for single-step, covalent labeling of the phosphate group of an organic substance under aqueous conditions are described. The labeling compound includes any kind of detectable signal group covalently bound to an imidazole moiety, which can be imidazole or a substituted imidazole. A preferred labeling compound has the formula I.

ST imidazole deriv prepn labeling organophosphate group; nucleotide labeling imidazole deriv; biopolymer labeling imidazole deriv; DNA adduct detn imidazole deriv label; phosphate group labeling imidazole compd

IT Dyes, azo
Fluorescent substances
Nucleic acid hybridization
Staining, biological
(1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)

IT Biopolymers
Nucleotides, analysis
Phosphate group
Phospholipids, analysis
Phosphoproteins
RL: **ANT (Analyte)**; **RCT (Reactant)**; ANST (Analytical study); **RACT (Reactant or reagent)**
(1-step signal group-imidazole **labeling** of organic phosphate groups under aqueous conditions)

IT Carbohydrates and Sugars, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)

IT Haptens
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)

IT Organometallic compounds
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)

IT Onium compounds
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(acridinium, esters, 1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)

IT **Deoxyribonucleic acids**
RL: **ANT (Analyte)**; ANST (Analytical study)
(**adducts**, 1-step signal group-imidazole **labeling** of organic phosphate groups under aqueous conditions)

IT Electrophoresis and Ionophoresis
(capillary, 1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)

IT Coordination compounds
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study); RACT (Reactant or reagent); USES (Uses)
(chelates, 1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)

IT Rare earth compounds
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(complexes, 1-step signal group-imidazole labeling of organic phosphate
groups under aqueous conditions)

IT Nucleotides, reactions
RL: ARG (Analytical reagent use); RCT (Reactant); ANST (Analytical study);
RACT (Reactant or reagent); USES (Uses)
(oligo-, 1-step signal group-imidazole labeling of organic phosphate
groups under aqueous conditions)

IT Nucleotides, analysis
RL: **ANT (Analyte)**; ANST (Analytical study)
(oligo-, deoxyribo-, 1-step signal group-imidazole **labeling**
of organic phosphate groups under aqueous conditions)

IT Amino acids, analysis
Carbohydrates and Sugars, analysis
RL: **ANT (Analyte)**; RCT (Reactant); ANST (Analytical study); RACT
(Reactant or reagent)
(phosphates, 1-step signal group-imidazole **labeling** of organic
phosphate groups under aqueous conditions)

IT Organic compounds, analysis
RL: **ANT (Analyte)**; RCT (Reactant); ANST (Analytical study); RACT
(Reactant or reagent)
(phosphorus-containing, 1-step signal group-imidazole **labeling** of
organic phosphate groups under aqueous conditions)

IT 365-07-1, 5'-TMP 653-63-4 902-04-5 1032-65-1 14490-86-9
148807-02-7 178388-84-6
RL: **ANT (Analyte)**; RCT (Reactant); ANST (Analytical study); RACT
(Reactant or reagent)
(1-step signal group-imidazole **labeling** of organic phosphate
groups under aqueous conditions)

IT 288-32-4, Imidazole, reactions **1672-46-4**, Digoxigenin
6788-84-7, Dioxetane 7273-34-9, Luciferin 7440-42-8D, Boron,
fluorophores containing 7782-41-4D, Fluorine, electrophores containing
10028-17-8, Tritium, reactions **14158-31-7**, Iodine-125,
reactions **14596-37-3**, Phosphorus-32, reactions
14762-75-5, Carbon-14, reactions **15117-53-0**, Sulfur-35,
reactions 15749-66-3, Phosphorus-33, reactions
RL: ARG (Analytical reagent use); **RCT (Reactant)**; ANST
(Analytical study); **RACT (Reactant or reagent)**; USES (Uses)
(1-step signal group-imidazole labeling of organic phosphate groups under
aqueous conditions)

IT 288-32-4DP, Imidazole, derivs. 151923-75-0P
RL: ARG (Analytical reagent use); RCT (Reactant); SPN (Synthetic
preparation); ANST (Analytical study); PREP (Preparation); RACT (Reactant
or reagent); USES (Uses)
(1-step signal group-imidazole labeling of organic phosphate groups under
aqueous conditions)

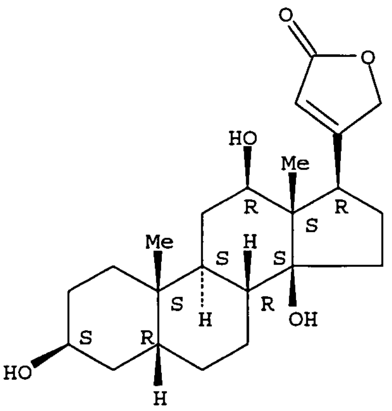
IT 178335-14-3P 178388-72-2P 178388-73-3P 178388-74-4DP, complex with
europium 178388-75-5P 178388-76-6P 178388-77-7P 178388-78-8P
178388-81-3P 178388-82-4P
RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST
(Analytical study); PREP (Preparation); USES (Uses)
(1-step signal group-imidazole labeling of organic phosphate groups under
aqueous conditions)

IT 107-15-3, 1,2-Ethanediamine, reactions 693-98-1, 2-Methylimidazole
2497-02-1, N-Acetyl-L-histidine 7440-53-1D, Europium, complex with
ethylenediamine ketoethylimidazole and isothiocyanate 82354-19-6
114932-60-4 124935-83-7 129273-26-3 178335-15-4 178388-71-1
178458-24-7
RL: RCT (Reactant); RACT (Reactant or reagent)
(1-step signal group-imidazole labeling of organic phosphate groups under
aqueous conditions)

IT 178388-79-9P, 1H-Imidazole-2-propanoic acid 178388-80-2P,
1H-Imidazole-2-butanoic acid
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)
(1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)
IT **1672-46-4**, Digoxigenin **10028-17-8**, Tritium, reactions
14158-31-7, Iodine-125, reactions **14596-37-3**,
Phosphorus-32, reactions **14762-75-5**, Carbon-14, reactions
15117-53-0, Sulfur-35, reactions
RL: ARG (Analytical reagent use); **RCT (Reactant)**; ANST
(Analytical study); **RACT (Reactant or reagent)**; USES (Uses)
(1-step signal group-imidazole labeling of organic phosphate groups under aqueous conditions)
RN 1672-46-4 HCAPLUS
CN Card-20(22)-enolide, 3,12,14-trihydroxy-, (3β,5β,12β)-
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 10028-17-8 HCAPLUS
CN Tritium (8CI, 9CI) (CA INDEX NAME)

T—T

RN 14158-31-7 HCAPLUS
CN Iodine, isotope of mass 125, at. (8CI, 9CI) (CA INDEX NAME)

^{125}I

RN 14596-37-3 HCAPLUS
CN Phosphorus, isotope of mass 32 (8CI, 9CI) (CA INDEX NAME)

^{32}P

RN 14762-75-5 HCAPLUS
CN Carbon, isotope of mass 14 (8CI, 9CI) (CA INDEX NAME)

^{14}C

RN 15117-53-0 HCAPLUS
CN Sulfur, isotope of mass 35 (8CI, 9CI) (CA INDEX NAME)

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35S


L95  ANSWER 15 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1995:827146  HCAPLUS
DN   123:250492
ED   Entered STN:  03 Oct 1995
TI   Quantitative measurement of sphingosine 1-phosphate in biological samples
     by acylation with radioactive acetic anhydride
AU   Yatomi, Yutaka; Ruan, Fuqiang; Ohta, Hideki; Welch, Robert J.; Hakomori,
     Sen-itiroh; Igarashi, Yasuyuki
CS   Biomembrane Inst., Seattle, WA, 98119, USA
SO   Analytical Biochemistry (1995), 230(2), 315-20
     CODEN: ANBCA2; ISSN: 0003-2697
PB   Academic
DT   Journal
LA   English
CC   9-8 (Biochemical Methods)
     Section cross-reference(s): 13
AB   A method was developed to quant. measure sphingosine 1-phosphate
     (Sph-1-P), a bioactive sphingolipid.  Sph-1-P was first extracted from cells
     into the upper aqueous phase under alkaline conditions by Folch's phase separation and
     then reextd. into the lower chloroform phase under acidic conditions.
     This phosphorylated sphingoid base extracted was quant. converted to
     N-[3H]-acetylated Sph-1-P, that is [3H]C2-ceramide 1-phosphate
     (C2-Cer-1-P), by N-acylation with [3H]acetic anhydride.  The
     [3H]C2-Cer-1-P formed by the acylation was resolved by TLC, detected with
     autoradiog., and quantitated by scraping the corresponding band and
     counting its radioactivity with a scintillation counter.  This assay
     allows quantification of Sph-1-P over a range from at least 100 pmol
     (often 30 pmol) to 10 nmol (the highest level tested).  The utility and
     validity of the assay were demonstrated by using human platelets.  The
     amount of Sph-1-P in platelet exts. was proportional to the cell number and
     calculated as 141 pmol/108 cells (mean), which was about four times higher
     than that of sphingosine.  The potent agonist thrombin did not affect the
     total Sph-1-P amts. in platelet suspensions but induced the release of
     Sph-1-P stored in the cells into the medium.
ST   platelet sphingosine phosphate detn radioassay
IT   Blood platelet
        (quant. determination of sphingosine 1-phosphate in biol. samples by acylation
        with radioactive acetic anhydride)
IT   169217-31-6P
     RL: ANT (Analyte); SPN (Synthetic preparation); ANST (Analytical
     study); PREP (Preparation)
        (quant. determination of sphingosine 1-phosphate in biol. samples by
        acylation with radioactive acetic anhydride)
IT   26993-30-6, Sphingosine 1-phosphate
     RL: BOC (Biological occurrence); BSU (Biological study, unclassified);
     BIOL (Biological study); OCCU (Occurrence)
        (quant. determination of sphingosine 1-phosphate in biol. samples by acylation
        with radioactive acetic anhydride)
IT   25962-31-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (quant. determination of sphingosine 1-phosphate in biol. samples by
        acylation with radioactive acetic anhydride)

L95  ANSWER 16 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1992:647570  HCAPLUS
DN   117:247570
ED   Entered STN:  26 Dec 1992
TI   Inhibition of sphingosine kinase in vitro and in platelets.  Implications
     for signal transduction pathways
AU   Buehrer, Benjamin M.; Bell, Robert M.
CS   Med. Cent., Duke Univ., Durham, NC, 27710, USA
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SO Journal of Biological Chemistry (1992), 267(5), 3154-9
CODEN: JBCHA3; ISSN: 0021-9258

DT Journal

LA English

CC 7-3 (Enzymes)
Section cross-reference(s): 13

AB Sphingosine kinase (I) was partially purified and characterized from rat brain microsomes. A new assay, utilizing octyl-β-D-glucopyranoside and sphingosine mixed micelles, was developed to quantitate formation of the product, sphingosine-1-phosphate. The assay was proportional with respect to time and protein, displayed Michaelis-Menten kinetics, and was subject to surface dilution with regard to sphingosine. Investigations of I substrate specificity showed that the enzyme was specific for the erythro-enantiomers of sphingosine and dihydrosphingosine. Neither of the threo-enantiomers were phosphorylated in this system, but both were found to be potent competitive inhibitors of I activity. Human blood platelet I activity displayed substrate and inhibitor specificities similar to the rat brain enzyme. A mixture of DL-threo-dihydrosphingosine competitively inhibited I activity in a dose-dependent manner in isolated platelets. DL-threo-Dihydrosphingosine caused a prolongation of the inhibition of thrombin-induced protein kinase C-dependent 40(47)-kDa protein phosphorylation in platelets. D-, L-, Or DL-threo-Dihydrosphingosine may be useful as a tool to investigate D-erythro-sphingosine metabolism and the function of sphingosine 1-phosphate in signal transduction processes.

ST sphingosine kinase inhibition brain platelet

IT Kinetics, enzymic
(of inhibition, of sphingosine kinase of rat brain microsomes)

IT Stereochemistry
(of sphingosine kinase reaction of brain microsome)

IT Michaelis constant
(of sphingosine kinase, of rat brain microsomes)

IT Brain, composition
(sphingosine kinase of microsomes of, of rat, determination and inhibition and characterization of)

IT Blood platelet
(sphingosine kinase of, of human, inhibition of, by dihydrosphingosine)

IT **50864-48-7**
RL: **ANT (Analyte)**; ANST (Analytical study)
(determination and inhibition and characterization of, of rat brain microsomes and human blood platelets)

IT **123-78-4**, D-Erythro-**Sphingosine** 3102-56-5
6036-75-5
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(reaction of, with **sphingosine** kinase of rat brain microsomes and human blood platelets, kinetics of)

IT 2304-75-8 6036-85-7 25695-95-8
RL: BIOL (Biological study)
(sphingosine kinase of rat brain microsomes and human blood platelet inhibition by, kinetics of)

IT **50864-48-7**
RL: **ANT (Analyte)**; ANST (Analytical study)
(determination and inhibition and characterization of, of rat brain microsomes and human blood platelets)

RN 50864-48-7 HCAPLUS

CN Kinase (phosphorylating), dihydrosphingosine (9CI) (CA INDEX NAME)

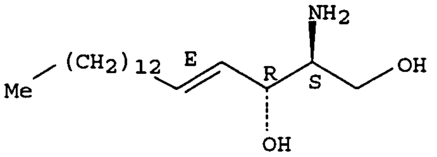
*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT **123-78-4**, D-Erythro-**Sphingosine** **6036-75-5**
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(reaction of, with **sphingosine** kinase of rat brain microsomes and human blood platelets, kinetics of)

RN 123-78-4 HCAPLUS

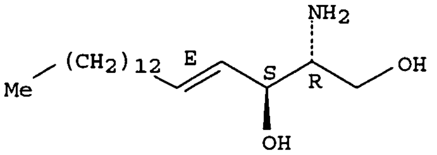
CN 4-Octadecene-1,3-diol, 2-amino-, (2S,3R,4E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).
Double bond geometry as shown.



RN 6036-75-5 HCAPLUS
CN 4-Octadecene-1,3-diol, 2-amino-, (2R,3S,4E)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).
Double bond geometry as shown.



L95 ANSWER 17 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1981:528686** HCAPLUS
DN 95:128686
ED Entered STN: 12 May 1984
TI Development of a quantitative assay for tissue levels of dolichyl phosphate
AU Keller, R. Kennedy; Tamkun, John W.; Adair, W. Lee, Jr.
CS Coll. Med., Univ. South Florida, Tampa, FL, 33612, USA
SO Biochemistry (**1981**), 20(20), 5831-6
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 13, 22
AB A sensitive assay is described for quantitating dolichyl phosphate (Dol-P), the polyprenyl phospholipid which participates in N-linked glycosylation. The assay is based on a novel reaction of alkyl phosphates with Ph chloroformate in which a monosubstituted mixed anhydride of phosphoric and carbonic acid is formed. Evidence in support of the proposed structure for the derivative includes a phosphate/phenyl ratio of 1, IR spectra, elemental anal., behavior during ion-exchange chromatog., and reactivity with primary and secondary amines. A simple, rapid procedure is described for the preparation of [14C]Ph chloroformate from [14C]phenol; use of the radiolabeled reagent allows assay of Dol-P in the subnanomole range. The assay was applied to the quantitation of total Dol-P levels in rat liver. Dol-P, Dol-PP, and their glycosylated derivs. were extracted with organic solvents and degraded to free Dol-P by acid hydrolysis. Following saponification to hydrolyze contaminating phospholipids, Dol-P was purified by using DEAE-cellulose chromatog. and derivatized with [14C]phenyl chloroformate. Tracer quantities of [3H]Dol-P were added to the tissue before extraction to monitor purification and yield. Double-label counting of the isolated derivative allowed calcn. of the level of total Dol-P in the original tissue sample. This procedure yielded values of 2.9 nmol Dol-P/g rat liver.
ST liver dolichyl phosphate detn; phenyl chloroformate dolichyl phosphate; radioassay dolichyl phosphate detn; alkyl phosphate reaction phenyl chloroformate
IT Liver, composition
(dolichyl phosphate determination in, by radioassay, carbon-14-labeled Ph chloroformate in)
IT **Phosphatidic acids**
Phosphatidylethanolamines

Phosphatidylglycerols
Phosphatidylserines
Phospholipids
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(reaction of, with Ph chloroformate)
IT 12698-55-4
RL: **ANT (Analyte)**; ANST (Analytical study)
(determination of, in liver by radioassay, carbon-14-**labeled** Ph chloroformate in)
IT 7244-85-1P 78894-71-0P
RL: PREP (Preparation)
(preparation and characterization of, dolichyl phosphate determination in relation to)
IT 78922-24-4P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and phosphorylation of)
IT 78922-23-3P
RL: PREP (Preparation)
(preparation of)
IT 78874-49-4P
RL: PREP (Preparation)
(preparation of, for dolichyl phosphate determination)
IT 78922-22-2P
RL: RCT (Reactant); PREP (Preparation); RACT (Reactant or reagent)
(purification and reduction of, by tritium-labeled borohydride)
IT 12751-23-4
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with Ph chloroformate)
IT 1885-14-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with dolichyl phosphate and other alkyl phosphates)
IT 75-44-5
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phenol or carbon-14-labeled phenol)
IT 108-95-2, reactions 37840-33-8
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with phosgene)

L95 ANSWER 18 OF 20 HCAPLUS COPYRIGHT 2005 ACS on STN
AN **1978:185637** HCAPLUS
DN 88:185637
ED Entered STN: 12 May 1984
TI Aspects of bradykinin radioimmunoassay
AU Odya, Charles E.; Goodfriend, Theodore L.; Stewart, John M.; Pena, Clara
CS Cent. Health Sci., Univ. Wisconsin, Madison, WI, USA
SO Journal of Immunological Methods (**1978**), 19(2-3), 243-57
CODEN: JIMMBG; ISSN: 0022-1759
DT Journal
LA English
CC 9-5 (Biochemical Methods)
Section cross-reference(s): 2
AB 125I-derivs. of Tyr1-kallidin, Tyr5-bradykinin, and Tyr8-bradykinin were prepared A technique for purification of the monoiodinated derivative is described. Bradykinin antiserums were tested for their ability to bind the mono-iodinated analogs. Each antiserum had a characteristic preference for 1 of the 3 labeled peptides. The sensitivity of each antiserum was greatest when it was used with the label bound most avidly by that antiserum. The specificity of an antiserum was not changed by varying the labeled analog. Some common enzyme inhibitors had significant effects on the antigen-antibody reactions. Lecithin interfered with the reaction between antiserum and Tyr1-kallidin. The data suggest that antiserums for bradykinin radioimmunoassay be tested with several radioactive iodobradykinins to maximize their usefulness. In addition, enzyme inhibitors used to stabilize levels of kinins in biol. fluids should be tested for their effects on the assay. Biol. samples rich in lipid may give spurious radioimmunoassay results unless they are freed of those phospholipids that

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     can bind labeled and unlabeled peptides.
ST   bradykinin detn; radioimmunoassay bradykinin peptide iodination
IT   Antibodies
     RL: ANST (Analytical study)
        (antigen reaction with, iodination of bradykinin analogs in relation
        to)
IT   Lecithins, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (inhibition by, of antiserum and iodinated bradykinin analogs in
        radioimmunoassay)
IT   Iodination
        (of bradykinin analogs, antiserum binding of)
IT   Antiserums
        (to bradykinin, iodinated bradykinin analogs binding to)
IT   Radiochemical analysis
        (immunol., iodinated analogs binding to antiserums in)
IT   Immunochemistry
        (radioimmunoassay, iodinated analogs binding to antiserums in)
IT   3316-27-6D, iodine-125 labeled derivs.   32222-00-7D, iodine-125 labeled
     derivs.   33289-76-8D, iodine-125 labeled derivs.
     RL: ANST (Analytical study)
        (antiserum binding by, in bradykinin radioimmunoassay)
IT   58-82-2
     RL: ANT (Analyte); ANST (Analytical study)
        (determination of, by radioimmunoassay, iodinated analogs in relation to)
IT   14158-31-7, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (labeling by, of bradykinin analogs, antiserum binding to)
IT   14158-31-7, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (labeling by, of bradykinin analogs, antiserum binding to)
RN   14158-31-7  HCAPLUS
CN   Iodine, isotope of mass 125, at. (8CI, 9CI)  (CA INDEX NAME)


125I


L95  ANSWER 19 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1978:47246  HCAPLUS
DN   88:47246
ED   Entered STN:  12 May 1984
TI   Radioimmunoassay reagent
IN   Polito, Alan J.; Knight, William S.
PA   Beckman Instruments, Inc., USA
SO   Ger. Offen., 21 pp.
     CODEN: GWXXBX
DT   Patent
LA   German
IC   C07J043-00
CC   9-5 (Biochemical Methods)
     Section cross-reference(s): 2
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.       DATE
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PI   DE 2720809           A1    19771201    DE 1977-2720809       19770509 <--
     AU 7724674           A1    19781102    AU 1977-24674         19770428 <--
     NL 7704846           A     19771114    NL 1977-4846          19770503 <--
     BE 854398            A1    19770901    BE 1977-177383        19770509 <--
     FR 2397426           A1    19790209    FR 1977-14099         19770509 <--
     JP 52136158          A2    19771114    JP 1977-52735         19770510 <--
PRAI US 1976-684688       A     19760510  <--
CLASS
 PATENT NO.      CLASS  PATENT FAMILY CLASSIFICATION CODES
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DE 2720809 IC C07J043-00

AB Reagents for radioimmunoassay are described that are prepared especially for the determination of steroids; the reagents are steroid derivs. that contain an imidazole group that can be labeled with a radioactive indicator such as 125I. These derivs. have the advantage that they have higher affinity for the antiserum and lower background counts in the counting vials than do the corresponding tyrosine derivs. Thus, cortisol 3-oxime (I) was prepared from 41.54 mg cortisol, 21.17 mg carboxymethylamine, and 41.43 mg NaOAc in 10 mL dry MeOH and purified by thin-layer chromatog. The cortisol 3-oxime-histamine derivative (II) was prepared after reaction of I with isobutylchloroformate. II then was iodinated with Na125I by using the Chloramine-T reaction. The corresponding aldosterone derivs. could be prepared by using the same methods. The determination of cortisol in blood serum is described.

ST cortisol detn reagent prepn; radioimmunoassay reagent steroid histamine deriv; steroid histamine deriv iodine 125 labeling; aldosterone detn histamine deriv

IT Blood analysis
(aldosterone and cortisol determination in, by radioimmunoassay, iodinated histamine derivs. in relation to)

IT 52-39-1
RL: **ANT (Analyte)**; ANST (Analytical study)
(determination of, iodinated histamine derivative preparation in relation to)

IT **14158-31-7**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(labeling by, of steroid oxime-histamine derivs. for radioimmunoassay)

IT 65418-86-2P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and iodination of, for aldosterone determination)

IT 65418-85-1P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and iodination of, for cortisol determination)

IT 65418-87-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, with histamine)

IT **50-23-7**
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(reaction of, with carboxymethylamine, cortisol determination in relation to)

IT 56-40-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cortisol)

IT 543-27-1
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, with cortisol 3-oxime)

IT 51-45-6, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction with steroid oxime derivs. and iodination of, for radioimmunoassay)

IT **14158-31-7**, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(labeling by, of steroid oxime-histamine derivs. for radioimmunoassay)

RN 14158-31-7 HCAPLUS

CN Iodine, isotope of mass 125, at. (8CI, 9CI) (CA INDEX NAME)

$^{125}\mathrm{I}$

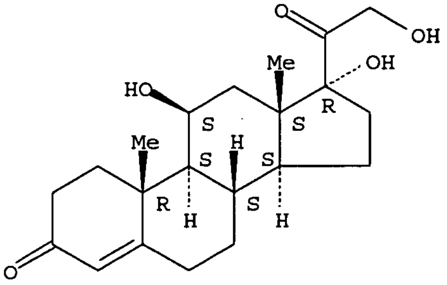
IT **50-23-7**
RL: **RCT (Reactant)**; **RACT (Reactant or reagent)**
(reaction of, with carboxymethylamine, cortisol determination in relation to)

RN 50-23-7 HCAPLUS

CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11β)- (9CI) (CA INDEX

NAME)

Absolute stereochemistry.



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L95  ANSWER 20 OF 20  HCAPLUS  COPYRIGHT 2005 ACS on STN
AN   1976:587540  HCAPLUS
DN   85:187540
ED   Entered STN:  12 May 1984
TI   Spin labeled compounds for use in forensic analysis
IN   Goldstein, Avram; Leute, Richard K.; Ullman, Edwin F.
PA   Syva Co., USA
SO   U.S., 46 pp. Continuation of U.S. 3,853,914.
     CODEN: USXXAM
DT   Patent
LA   English
IC   C07D451-12
INCL 260292000
CC   4-2 (Toxicology)
     Section cross-reference(s): 1
FAN.CNT 5
     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     ---------------     ----   --------    --------------------   --------
PI   US 3966744           A     19760629    US 1974-482542         19740624 <--
     US 3690834           A     19720912    US 1971-141516         19710510 <--
     FR 2121723           A5    19720825    FR 1972-687            19720110 <--
     FR 2121723           B1    19730629
     US 3853914           A     19741210    US 1972-270108         19720710 <--
PRAI US 1971-105535       A2    19710111  <--
     US 1971-141516       A2    19710510  <--
     US 1972-270108       A1    19720710  <--
CLASS
 PATENT NO.       CLASS  PATENT FAMILY CLASSIFICATION CODES
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 US 3966744       IC     C07D451-12
                  INCL   260292000
 US 3966744       NCL    546/125.000; 546/022.000; 546/044.000; 546/074.000;
                         546/079.000; 546/112.000; 546/188.000; 546/210.000;
                         546/219.000; 546/229.000; 546/244.000; 546/278.400  <--
 US 3690834       NCL    436/537.000; 422/050.000; 435/006.000; 435/007.800;
                         435/188.000; 436/803.000; 436/816.000; 436/817.000;
                         530/363.000; 530/389.800; 530/403.000; 530/404.000;
                         530/405.000; 530/406.000; 530/408.000; 530/409.000;
                         530/410.000; 544/035.000; 544/041.000; 544/044.000;
                         544/243.000; 544/260.000; 544/302.000; 546/024.000;
                         546/044.000; 546/069.000; 546/125.000; 546/189.000;
                         546/196.000; 546/201.000; 546/208.000; 546/216.000;
                         546/223.000; 546/225.000; 546/228.000; 548/504.000;
                         548/542.000                                         <--
 US 3853914       NCL    548/542.000; 436/086.000; 436/128.000; 436/173.000;
                         544/179.000; 546/190.000; 546/191.000; 546/208.000;
                         546/223.000; 546/224.000; 546/229.000; 546/232.000;
                         546/234.000; 548/233.000; 548/300.100; 548/316.700;
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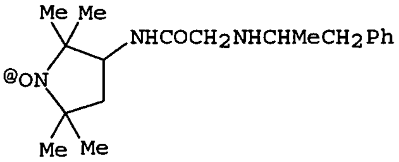
548/331.500; 548/333.500; 548/347.100; 548/350.100;
548/351.100; 548/352.100; 548/354.100 <--

GI



II

AB Spin labeled compds. (ligand analogs) for use in forensic immunoassay were prepared by modifying biol. active compds. or structural analogs and coupling them with a stable free radical compound The ligand analog is recognizable by receptor mol., usually on antibody, and can compete with a biol. active mol. (ligand) for the receptor site in a way which allows the biol. active mol. to be assayed spectrometrically. For example, 2 mmoles amphetamine (I) [300-62-9] in 20 ml MeOH was treated with 106 mg Na2CO3 [497-19-8] and 321 mg 3-(2'-iodoacetamido)-2,2,5,5-tetramethyl-1-pyrrolidinyl-1-oxyl [27048-01-7] to give 187 mg 3-(N-(1'-phenyl-2'-propyl)glycinamido)-2,2,5,5-tetramethylpyrrolidinyl-1-oxyl (II) [41370-71-2]. The Et2O extract of a solution of 3.68 g amphetamine sulfate [60-13-9] in 80 ml 0.5N NaOH was evaporated, and the residue was dissolved in 50 ml benzene and treated with 3 ml diisopropylethylamine [7087-68-5] and 2.2 ml Et bromoacetate [105-36-2] to give the amino ester. The ester was dissolved in 50 ml 1:1 MeOH-1N NaOH, and the solution was concentrated, and treated with HCl to pH 6 to give 900 mg N-carboxymethyl amphetamine [7738-39-8]. A suspension of the acid (700 mg) in 50 ml dry dioxane was treated with 20 ml of 12.5% phosgene in benzene, and the mixture was evaporated, redissolved in 20 ml/dry dioxane, and added over .5 hr to 2 g bovine serum albumin in 100 ml 2% NaHCO3 at 0°. After 24 hr at 0° and 18 hr at room temperature, the reaction mixture was dialyzed for 2 days against 35 l H2O at 0°, and lyophilized, giving 1.91 g conjugate containing .apprx.76 I units per unit of albumin. For urine anal. for I, 25 μl urine was mixed with 2.5 μl 0.2M Na2Cr2O7 and added to a mixture of 22 μl I antibody (γ-globulin), 144 μl 2M pH8 borate buffer, and 99 μl saline. Five μl of a solution of 105 μl H2O and 160 μl 2.8 + 10-5M I solution was added, and the solution was examined by ESR spectroscopy. The method detected I concns. in the range of 0.7-1.5 μg/ml. It also detected several other drugs with structures similar to I.

ST urine drug analysis forensic; spin label drug urine analysis

IT Albumins, blood serum
RL: BIOL (Biological study)
(bovine, ligand analogs conjugation with)

IT Legal chemistry and medicine
(drug determination in urine in, spin-labeled compds. for)

IT Urine analysis
(drug determination in, spin-labeled compds. for)

IT 8-Azabicyclo[3.2.1]octane-2-carboxylic acid, 3-hydroxy-8-methyl-, [1R-(exo,exo)]-, albumin conjugates
8-Azabicyclo[3.2.1]octane-8-acetic acid, 3-(benzoyloxy)-2-(methoxycarbonyl)-, [1R-(exo,exo)]-, albumin conjugates
Benzenediazonium, 4-[(2-carboxy-3-hydroxy-8-azabicyclo[3.2.1]oct-8-yl)methyl]-, [1R-(exo,exo)]-, albumin conjugates
Benzenediazonium, 4-[[(2-carboxy-8-methyl-8-azabicyclo[3.2.1]oct-3-yl)oxy]carbonyl]-, hydroxide, inner salt, [1R-(exo,exo)]-, albumin conjugates
Benzenediazonium, 4-[[3-hydroxy-2-(methoxycarbonyl)-8-azabicyclo[3.2.1]oct-8-yl]methyl]-, [1R-(exo,exo)]-, albumin conjugates
L-Lysine, homopolymer, hydrobromide, carboxymethylmorphine conjugates
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of)

IT 57-30-7

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     RL: RCT (Reactant); RACT (Reactant or reagent)
        (carboxyethylation of)
IT   50-28-2, biological studies   77-21-4   309-43-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (carboxymethylation of)
IT   60426-41-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (debenzylation of)
IT   50-06-6, analysis   50-11-3   50-53-3, analysis   51-57-0   57-33-0
     57-42-1   57-43-2   64-04-0   71-73-8   76-99-3   100-92-5   115-38-8
     125-71-3   154-41-6   309-43-3   1007-33-6   1212-72-2   2706-50-5
     5411-22-3
     RL: ANT (Analyte); ANST (Analytical study)
        (detection of, in urine, by ESR with spin-labeled compds.)
IT   50-13-5   5796-31-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (esterification of)
IT   51304-58-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (hydrolysis of)
IT   3434-88-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (oxidation of)
IT   56740-97-7P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and acetylation of)
IT   7738-39-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and albumin conjugation of)
IT   77-17-8P   466-97-7P   18717-72-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and carboxymethylation of)
IT   20827-47-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and deacetylation of)
IT   56740-96-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and decarbamoylation of)
IT   60343-20-6P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and deesterification of)
IT   57116-54-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and diazotation of)
IT   60343-29-5P   60343-32-0P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydrogenation of)
IT   56740-95-5P   60342-90-7P   60342-95-2P   60343-43-3P   60546-87-4P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and hydrolysis of)
IT   60343-37-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and methoxylation of)
IT   60343-23-9P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and nitrobenzylation of)
IT   3627-45-0P
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     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and oxidation of)
IT   58109-31-2P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and reduction of)
IT   3434-45-5P   3627-48-3DP, 4-Piperidinecarboxylic acid, 1-methyl-4-phenyl-,
     bovine serum albumin conjugates   19209-45-1DP, 1-Piperidineacetic acid,
     4-(ethoxycarbonyl)-4-phenyl-, albumin conjugates   19209-45-1P
     19823-38-2P   24749-37-9DP, Estrane, acetic acid derivative, albumin
     conjugates   24749-37-9DP, Estrane, acetic acid derivative, albumin conjugates
     35048-47-6DP, Acetic acid, [[[(17β)-3,17-dihydroxyestra-1,3,5(10)-
     trien-6-ylidene]amino]oxy]-, albumin conjugates   39038-18-1P
     41164-36-7DP, Acetic acid, [[(17β)-17-hydroxyestra-1,3,5(10)-trien-3-
     yl]oxy]-, albumin conjugates   41370-61-0P   41370-62-1P   41370-63-2P
     41370-64-3P   41370-68-7P   41370-69-8P   41370-71-2P   55605-46-4DP,
     2-Butenoic acid, 4-[hexahydro-5-(1-methylbutyl)-2,4,6-trioxo-5-
     pyrimidinyl]-, albumin conjugates   55605-46-4P   55605-47-5DP,
     1-Piperidineacetic acid, 3-ethyl-2,6-dioxo-3-phenyl-, albumin conjugates
     55605-47-5P   55605-49-7P   55738-78-8P   55738-83-5P   57116-56-0P
     59957-85-6P   60342-87-2P   60342-89-4P   60342-91-8P   60342-92-9P
     60342-97-4P   60342-98-5P   60342-99-6P   60343-00-2P   60343-02-4DP,
     Acetic acid, [4-[2-[(trifluoroacetyl)amino]propyl]phenoxy]-, anhydride
     with carbonochloridic acid, albumin conjugates   60343-03-5P   60343-04-6P
     60343-05-7P   60343-06-8DP, Benzenebutanoic acid, β-(methylamino)-,
     albumin conjugates   60343-06-8P   60343-08-0DP, Acetic acid,
     [4-(2-aminopropyl)phenoxy]-, albumin conjugates   60343-09-1P
     60343-10-4P   60343-11-5P   60343-12-6P   60343-13-7P   60343-16-0P
     60343-17-1P   60343-18-2P   60343-19-3DP, 1-Pyrrolidinyloxy,
     3-[[9-(dimethylamino)-1,6-dioxo-7,7-diphenyldecyl]amino]-2,2,5,5-
     tetramethyl-, albumin conjugates   60343-19-3P   60343-22-8P   60343-24-0P
     60343-26-2P   60343-30-8P   60343-33-1P   60343-35-3P   60343-36-4P
     60343-39-7P   60343-42-2P   60546-94-3P   131027-32-2DP, Acetic acid,
     [4-[2-(methylamino)propyl]phenoxy]-, albumin conjugates
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of)
IT   7738-39-8DP, Glycine, N-(1-methyl-2-phenylethyl)-, albumin conjugates
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and antibody formation by)
IT   60342-93-0P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and conversion to acid chloride)
IT   55738-76-6P   60343-14-8P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation of and hydrolysis of)
IT   60342-94-1P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with amino tetramethylpropyrrolidinyloxyl)
IT   55738-79-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with aminotetramethylpyrrolidinyloxy and
        isobutylchloroformate)
IT   60342-86-1P   60343-38-6P   60343-41-1P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with aminotetramethylpyrrolidinyloxyl)
IT   35048-47-6P   56740-98-8P   60342-96-3P   60343-15-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with aminotetramethylpyrrolidinyloxyl and
        dicyclohexylcarbodiimide)
IT   60342-88-3P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with aminotetramethylpyrrolidinyloxyl and
        isobutylchloroformate)
IT   60343-21-7P
```

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     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with aminotetramethyltetramethylpyrrolidinyloxy
        and dicyclohexylcarbodiimide)
IT   57116-53-7P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with carboxyoxyltetramethylpyrrolidine)
IT   60343-25-1P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with carboxytetramethylpyrrolidine oxyl and
        isobutylchloroformate)
IT   561-27-3P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with cyanogen bromide)
IT   27809-64-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with iodoacetamidotetramethylpyrrolidinyloxyl
        and sodium hydride)
IT   7143-09-1P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with nitrobenzoyl chloride)
IT   3627-48-3P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with phenyl chloride and amino
        tetramethylpyrrolidinyloxyl)
IT   60343-40-0P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of and reaction with thiophosgene)
IT   1428-66-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with amino tetramethylpyrrolidinyloxy and
        dicyclohexylcarbodiimide)
IT   2154-67-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with aminobenzyl norecgonine methyl ester dihydrochloride
        and isobutylchloroformate)
IT   407-25-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with aminopropylphenoxyacetic acid)
IT   121-44-8, biological studies
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with aminotetramethylpyrrolidinyloxyl and
        diacetylcarboxymethylnormorphine and isobutylchloroformate)
IT   41093-72-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with aminotetramethylpyrrolidinyloxyl and
        isobutylchloroformate)
IT   6065-32-3   14660-52-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with amphetamine and diisopropylethylamine)
IT   497-19-8, biological studies
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with amphetamine and iodoacetamidotetramethylpyrrolidinyl
        oxyl)
IT   105-36-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with amphetamine sulfate and diisopropylethylamine)
IT   7087-68-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with amphetamine sulfate and esters)
IT   7087-68-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with benzylbromovalerate and norcocaine)
IT   77-17-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with bromoacetamidotetramethylpyrrolidinyloxyl)
IT   2154-68-9   24567-97-3
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     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with carbethoxyphenylpiperidine)
IT   571-92-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with carboxymethylhydroxylamine hemihydrochloride)
IT   538-75-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with diacetylcarboxymethylnormorphine)
IT   60343-28-4
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with diisopropylethyl amine and norcocaine)
IT   60343-31-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with diisopropylethylene amine and norcocaine)
IT   309-43-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with dimethylsulfide and ozone)
IT   55775-29-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with dinitrochlorobenzene)
IT   14691-88-4   55738-73-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with dinitrofluorobenzene)
IT   110-52-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with diphenyldimethylaminovaleronitrile)
IT   122-04-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with ecgonine methyl ester)
IT   60-13-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with esters and free radical spin-labeling compds.)
IT   70-34-8   77-17-8   300-62-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with free radical spin-labeling compds.)
IT   506-68-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with heroin)
IT   407-25-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with hydroxyamphetamine hydrobromide)
IT   60343-07-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with isobutylchloroformate and triethylamine)
IT   543-27-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with ligands and spin-labeling compds.)
IT   27048-01-7   34272-83-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with ligands, in spin-labeled ligand analog preparation)
IT   57-30-7
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with methylchloroacetate)
IT   122-78-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with monoethyl malonate)
IT   3196-15-4   3926-62-3   17932-40-0   24567-97-3   26330-51-8   54049-24-0
     55738-75-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with morphine)
IT   100-11-8
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with norecgonine methyl ester)
IT   1068-52-6
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with normorphine)
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IT   20295-82-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with oxoestradiol)
IT   75-18-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with ozone and sodium secobarbital)
IT   1071-46-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with phenylacetaldehyde)
IT   593-51-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with phenyllevulinic acid)
IT   96-34-4   535-11-5   6065-32-3
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with sodium phenobarbital)
IT   125-79-1
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with tetramethylene dibromide)
IT   96-34-4
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, with trifluoroacetylhydroxyamphetamine)
IT   306-21-8   60343-08-0
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (trifluoroacetylation of)
IT   10028-15-6, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (with dimethylsulfide and sodium secobarbital)
IT   57-27-2, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (with free radical spin-labeling compds.)
IT   50-28-2, biological studies
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (carboxymethylation of)
RN   50-28-2  HCAPLUS
CN   Estra-1,3,5(10)-triene-3,17-diol (17β)- (9CI)  (CA INDEX NAME)

Absolute stereochemistry.
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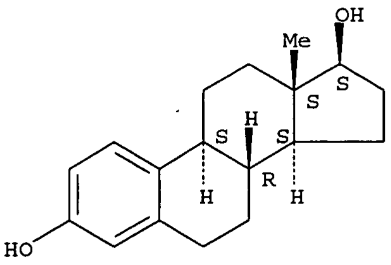

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=> b biosis
FILE 'BIOSIS' ENTERED AT 11:16:46 ON 23 JUN 2005
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FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 16 June 2005 (20050616/ED)

FILE RELOADED: 19 October 2003.

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L80 ANSWER 1 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2004:327010 BIOSIS

DN PREV200400328655

TI Apolipoprotein A-I-stimulated apolipoprotein E secretion from human macrophages is independent of cholesterol efflux.

AU Kockx, Maaike; **Rye, Kerry-Anne**; Gaus, Katharina; Quinn, Carmel M.; Wright, Janelle; Sloane, Timothy; Sviridov, Dimitri; Fu, Ying; Sullivan, David; Burnett, John R.; Rust, Stephan; Assmann, Gerd; Anantharamaiah, G. M.; Palgunachari, Mayakonda N.; Katz, Sissel Lund; Phillips, Michael C.; Dean, Roger T.; Jessup, Wendy; Kritharides, Leonard [Reprint Author]

CS Ctr Vasc ResMacrophage Biol Grp, Univ New S Wales, 4th Floor Wallace Wurth Bldg, Sydney, NSW, 2052, Australia
l.kritharides@unsw.edu.au

SO Journal of Biological Chemistry, (June 18 2004) Vol. 279, No. 25, pp. 25966-25977. print.
CODEN: JBCHA3. ISSN: 0021-9258.

DT Article

LA English

ED Entered STN: 29 Jul 2004
Last Updated on STN: 29 Jul 2004

AB Apolipoprotein A-I (apoA-I)-mediated cholesterol efflux involves the binding of apoA-I to the plasma membrane via its C terminus and requires **cellular** ATP-binding cassette transporter (ABCA1) activity. ApoA-I also stimulates secretion of apolipoprotein E (apoE) from macrophage foam **cells**, although the mechanism of this process is not understood. In this study, we demonstrate that apoA-I stimulates secretion of apoE independently of both ABCA1-mediated cholesterol efflux and of **lipid** binding by its C terminus. Pulse-chase experiments using 35S-**labeled cellular** apoE demonstrate that macrophage apoE exists in both relatively mobile (Em) and stable (Es) pools, that apoA-I diverts apoE from degradation to secretion, and that only a small proportion of apoA-I-mobilized apoE is derived from the **cell** surface. The structural requirements for induction of apoE secretion and cholesterol efflux are clearly dissociated, as C-terminal deletions in recombinant apoA-I reduce cholesterol efflux but increase apoE secretion, and deletion of central helices 5 and 6 decreases apoE secretion without perturbing cholesterol efflux. Moreover, a range of 11- and 22-mer alpha-helical peptides representing amphipathic alpha-helical segments of apoA-I stimulate apoE secretion whereas only the C-terminal alpha-helix (domains 220 - 241) stimulates cholesterol efflux. Other alpha-helix-containing apolipoproteins (apoA-II, apoA-IV, apoE2, apoE3, apoE4) also stimulate apoE secretion, implying a positive feedback autocrine loop for apoE secretion, although apoE4 is less effective. Finally, apoA-I stimulates apoE secretion normally from macrophages of two unrelated subjects with genetically confirmed Tangier Disease (mutations C733R and c. 5220 - 5222delTCT; and mutations A1046D and c. 4629 - 4630insA), despite severely inhibited cholesterol efflux. We conclude that apoA-I stimulates secretion of apoE independently of cholesterol efflux, and that this represents a novel, ABCA-1-independent, positive feedback pathway for stimulation of potentially anti-atherogenic apoE secretion by alpha-helix-containing molecules including apoA-I and apoE.

CC Cytology - Animal 02506
Cytology - Human 02508
Genetics - Human 03508
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Sterols and steroids 10067
Biophysics - Membrane phenomena 10508
Pathology - General 12502
Metabolism - Metabolic disorders 13020
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004
Morphology and cytology of bacteria 30500
Physiology and biochemistry of bacteria 31000
Immunology - General and methods 34502

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IT    Major Concepts
         Biochemistry and Molecular Biophysics; Immune System (Chemical
         Coordination and Homeostasis); Membranes (Cell Biology)
IT    Parts, Structures, & Systems of Organisms
         foam cells: immune system; macrophages: blood and lymphatics,
         immune system; plasma membrane
IT    Diseases
         Tangier Disease: genetic disease, metabolic disease, pathology
         Tangier Disease (MeSH)
IT    Chemicals & Biochemicals
         11-mer alpha-helical peptides; 22-mer alpha-helical peptides;
         ATP-binding cassette transporter [ABCA1]: activity; apolipoprotein A-I:
         carboxy-terminus; apolipoprotein E: secretion; cholesterol: efflux
IT    Methods & Equipment
         pulse-chase experiment: laboratory techniques
ORGN  Classifier
         Enterobacteriaceae   06702
      Super Taxa
         Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria;
         Microorganisms
      Organism Name
         Escherichia coli (species): expression system, strain-B121-DE3
      Taxa Notes
         Bacteria, Eubacteria, Microorganisms
ORGN  Classifier
         Hominidae   86215
      Super Taxa
         Primates; Mammalia; Vertebrata; Chordata; Animalia
      Organism Name
         human (common)
      Taxa Notes
         Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN    57-88-5 (cholesterol)

L80   ANSWER 2 OF 12  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
AN    2004:284709  BIOSIS
DN    PREV200400288028
TI    High-density lipoproteins neutralize C-reactive protein proinflammatory
      activity.
AU    Wadham, Carol; Albanese, Nathaniel; Roberts, Jane; Wang, Lijun; Bagley,
      Christopher J.; Gamble, Jennifer R.; Rye, Kerry-Anne;
      Barter, Philip J.; Vadas, Mathew A.; Xia, Pu
      [Reprint Author]
CS    no org, Frome Rd,POB 14 Rundle Mall, Adelaide, SA, 5000, Australia
      pu.xia@imvs.sa.gov.au
SO    Circulation, (May 4 2004) Vol. 109, No. 17, pp. 2116-2122. print.
      ISSN: 0009-7322 (ISSN print).
DT    Article
LA    English
ED    Entered STN: 16 Jun 2004
      Last Updated on STN: 16 Jun 2004
AB    Background-C-reactive protein (CRP), a well-recognized marker of
      atherosclerosis, has recently been suggested to have a direct
      proinflammatory effect.  The constitutive expression of low levels of CRP
      in normal plasma suggests the likelihood that a natural factor exists to
      neutralize the effect of CRP.  This factor(s) has not yet been identified.
      Method and Results - The proinflammatory effect of CRP was measured by the
      induction of inflammatory adhesion molecules in human umbilical vein
      endothelial cells (HUVECs).  We show that CRP significantly
      induced upregulation of adhesion molecules in both protein and mRNA
      levels.  The CRP-induced expression of these inflammatory adhesion
      molecules was completely suppressed when the cells were
      preincubated with a physiological concentration ( 1 mg/mL apolipoprotein
      A-I) of HDLs derived from human plasma (native HDL) or reconstituted HDL
      (rHDL) at a very low concentration (0.01 mg/mL apolipoprotein A-I).  A
      novel mechanism of HDL inhibition is likely to operate, because ( 1) rHDL
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     was 100 times more potent than native HDL, ( 2) preincubation with HDL and
     its sustained presence were obligatory, and ( 3) oxidized
     1-palmitoyl-2-linoleoyl-sn-glycero-3-phosphocholine was the fundamental
     active component.  Conclusions - The CRP-induced upregulation of
     inflammatory adhesion molecules in HUVECs was completely prevented by HDL
     via their oxidized phospholipid components.
CC   Biochemistry studies - General   10060
     Biochemistry studies - Proteins, peptides and amino acids   10064
     Biochemistry studies - Lipids   10066
     Cardiovascular system - Physiology and biochemistry   14504
     Cardiovascular system - Blood vessel pathology   14508
IT   Major Concepts
        Biochemistry and Molecular Biophysics; Cardiovascular System (Transport
        and Circulation)
IT   Diseases
        atherosclerosis: vascular disease
        Arteriosclerosis (MeSH)
IT   Chemicals & Biochemicals
        1-palmitoyl-2-linoleoyl-sn-glycero-3-phosphocholine; C-reactive
        protein; high-density lipoprotein
ORGN Classifier
        Hominidae   86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        HUVEC cell line (cell line): human umbilical vein
        endothelial cells
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L80  ANSWER 3 OF 12  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
AN   2004:234963  BIOSIS
DN   PREV200400235026
TI   Formation and metabolism of prebeta-migrating, lipid-poor
     apolipoprotein A-I.
AU   Rye, Kerry-Anne; Barter, Philip J. [Reprint Author]
CS   The Heart Research Institute, 145 Missenden Rd, Camperdown, Sydney, NSW,
     2050, Australia
     p.barter@hri.org.au
SO   Arteriosclerosis Thrombosis and Vascular Biology, (March 2004) Vol. 24,
     No. 3, pp. 421-428. print.
     ISSN: 1079-5642 (ISSN print).
DT   Article
LA   English
ED   Entered STN: 28 Apr 2004
     Last Updated on STN: 28 Apr 2004
AB   The preferred extracellular acceptor of cell
     phospholipids and unesterified cholesterol in the process mediated
     by the ATP-binding cassette A1 (ABCA1) transporter is a monomolecular,
     prebeta-migrating, lipid-poor or lipid-free form of
     apolipoprotein (apo) A-I.  This monomolecular form of apoA-I is quite
     distinct from the prebeta-migrating, discoidal high-density lipoprotein
     (HDL) that contains two or three molecules of apoA-I per particle and
     which are present as minor components of the HDL fraction in human plasma.
     The mechanism of the ABCA1-mediated efflux of phospholipid and
     cholesterol from cells has been studied extensively.  In
     contrast, much less attention has been given to the origin and subsequent
     metabolism of the acceptor lipid-free/lipid-poor
     apoA-I.  There is a substantial body of evidence from studies conducted in
     vitro that a monomolecular, lipid-free/lipid-poor form
     of apoA-I dissociates from HDL during the remodeling of HDLs by plasma
     factors such as cholesteryl ester transfer protein, hepatic lipase, and
     phospholipid transfer protein.  The rate at which apoA-I
     dissociates from HDL is influenced by the phospholipid
     composition of the particles and by the presence of apoA-II.  This review
     describes current knowledge regarding the formation, metabolism, and
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regulation of monomolecular, **lipid**-free/**lipid**-poor
apoA-I in plasma.

CC Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biochemistry studies - Sterols and steroids 10067
Metabolism - General metabolism and metabolic pathways 13002
Blood - Blood and lymph studies 15002
Blood - Blood cell studies 15004

IT Major Concepts
Metabolism

IT Parts, Structures, & Systems of Organisms
plasma: blood and lymphatics

IT Chemicals & Biochemicals
ATP-binding cassette A1 [ABCA1]: **biomarker**; apolipoprotein A-I: **biomarker**, monomolecular form, prebeta migrating **lipid** free/**lipid** poor form, metabolism, regulation; apolipoprotein A-II: **biomarker**; cholesterol; cholesteryl ester transfer protein: **biomarker**; hepatic lipase: **biomarker**; high-density lipoprotein: **biomarker**, prebeta-migrating discoidal; **phospholipid**; **phospholipid** transfer protein: **biomarker**

IT Miscellaneous Descriptors
reverse cholesterol transport pathway

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common)
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 57-88-5 (cholesterol)
9001-62-1 (hepatic lipase)

L80 ANSWER 4 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2003:83883 BIOSIS
DN PREV200300083883
TI The nucleotide-binding site of human **sphingosine** kinase 1.
AU **Pitson, Stuart M.** [Reprint Author]; Moretti, Paul A. B.; Zebol, Julia R.; Zareie, Reza; Derian, Claudia K.; Darrow, Andrew L.; Qi, Jenson; D'Andrea, Richard J.; Bagley, Christopher J.; **Vadas, Mathew A.**; Wattenberg, Binks W.
CS Div. of Human Immunology, Hanson Institute, Inst. of Medical and Veterinary Science, Frome Rd., Adelaide, SA, 5000, Australia
stuart.pitson@imvs.sa.gov.au
SO Journal of Biological Chemistry, (December 20 2002) Vol. 277, No. 51, pp. 49545-49553. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English
ED Entered STN: 6 Feb 2003
Last Updated on STN: 6 Feb 2003

AB **Sphingosine** kinase catalyzes the formation of **sphingosine** 1-phosphate, a **lipid** second messenger that has been implicated in a number of agonist-driven **cellular** responses including mitogenesis, anti-apoptosis, and expression of inflammatory molecules. Despite the importance of **sphingosine** kinase, very little is known regarding its structure or mechanism of catalysis. Moreover, **sphingosine** kinase does not contain recognizable catalytic or substrate-binding sites, based on sequence motifs found in other kinases. Here we have elucidated the nucleotide-binding site of human **sphingosine** kinase 1 (hSK1) through a combination of site-directed mutagenesis and affinity **labeling** with the ATP analogue, FSBA. We have shown that Gly82 of hSK1 is involved in ATP binding since mutation of this residue to alanine resulted in an enzyme with an apprx45-fold higher Km(ATP). We have also

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     shown that Lys103 is important in catalysis since an alanine substitution
     of this residue ablates catalytic activity.  Furthermore, we have shown
     that this residue is covalently modified by FSBA.  Our data, combined with
     amino acid sequence comparison, suggest a motif of SGDGX17-21K is involved
     in nucleotide binding in the sphingosine kinases.  This motif
     differs in primary sequence from all previously identified
     nucleotide-binding sites.  It does, however, share some sequence and
     likely structural similarity with the highly conserved glycine-rich loop,
     which is known to be involved in anchoring and positioning the nucleotide
     in the catalytic site of many protein kinases.
CC   Genetics - Animal   03506
     Biochemistry studies - Nucleic acids, purines and pyrimidines   10062
     Enzymes - General and comparative studies: coenzymes   10802
     Metabolism - General metabolism and metabolic pathways   13002
IT   Major Concepts
        Enzymology (Biochemistry and Molecular Biophysics); Metabolism
IT   Chemicals & Biochemicals
        5'-p-fluorosulfonylbenzoyladenosine: ATP analogue; sphingosine
        1-phosphate; sphingosine kinase 1: nucleotide-binding site
IT   Miscellaneous Descriptors
        nucleotide sequence
ORGN Classifier
        Hominidae   86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        human (common)
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN   57454-44-1 (5'-p-fluorosulfonylbenzoyladenosine)
     26993-30-6 (sphingosine 1-phosphate)

L80  ANSWER 5 OF 12  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
AN   2002:68439  BIOSIS
DN   PREV200200068439
TI   A point mutant of human sphingosine kinase 1 with increased
     catalytic activity.
AU   Pitson, Stuart M. [Reprint author]; Moretti, Paul A. B.; Zebol,
     Julia R.; Vadas, Mathew A.; D'Andrea, Richard J.; Wattenberg,
     Binks W.
CS   Hanson Centre for Cancer Research, Division of Human Immunology, Institute
     of Medical and Veterinary Science, Frome Road, Adelaide, SA, 5000,
     Australia
     stuart.pitson@imvs.sa.gov.au
SO   FEBS Letters, (7 December, 2001) Vol. 509, No. 2, pp. 169-173. print.
     CODEN: FEBLAL. ISSN: 0014-5793.
DT   Article
LA   English
OS   Genbank-AF200328
ED   Entered STN: 16 Jan 2002
     Last Updated on STN: 21 Mar 2002
AB   Sphingosine kinase (SK) catalyses the formation of
     sphingosine 1-phosphate, a lipid second messenger that
     has been implicated in mediating such fundamental biological processes as
     cell growth and survival.  Very little is currently known
     regarding the structure or mechanisms of catalysis and activation of SK.
     Here we have tested the functional importance of Gly113, a highly
     conserved residue of human sphingosine kinase 1 (hSK), by
     site-directed mutagenesis.  Surprisingly, a Gly113fwdarwAla substitution
     generated a mutant that had 1.7-fold greater catalytic activity than
     wild-type hSK (hSKWT).  Our data suggests that the Gly113fwdarwAla
     mutation increases catalytic efficiency of hSK, probably by inducing a
     conformational change that increases the efficiency of phosphoryl
     transfer.  Interestingly, hSKG113A activity could be stimulated in HEK293T
     cells by cell agonists to a comparable extent to hSKWT.
CC   Cytology - General   02502
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     Cytology - Human   02508
     Genetics - General   03502
     Genetics - Animal   03506
     Genetics - Human   03508
     Biochemistry studies - Nucleic acids, purines and pyrimidines   10062
     Biochemistry studies - Proteins, peptides and amino acids   10064
     Enzymes - General and comparative studies: coenzymes   10802
IT   Major Concepts
          Cell Biology; Enzymology (Biochemistry and Molecular
        Biophysics); Molecular Genetics (Biochemistry and Molecular Biophysics)
IT   Chemicals & Biochemicals
          sphingosine kinase 1: catalytic activity, point mutation;
        sphingosine-1-phosphate
IT   Sequence Data
        AF200328: Genbank, nucleotide sequence
IT   Methods & Equipment
        Western blotting: detection method, labeling; site-directed
        mutagenesis: genetic method, mutagenesis/deletion
IT   Miscellaneous Descriptors
        molecular sequence data
ORGN Classifier
        Hominidae   86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Organism Name
        HEK293T cell line: human embryonic kidney cells,
        transfected
        human
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN   26993-30-6 (sphingosine-1-phosphate)
     287713-61-5 (GENBANK-AF200328)

L80  ANSWER 6 OF 12  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
AN   2000:466126  BIOSIS
DN   PREV200000466126
TI   Human sphingosine kinase: Purification, molecular cloning and
     characterization of the native and recombinant enzymes.
AU   Pitson, Stuart M.; D'Andrea, Richard J.; Vandeleur, Lucianne;
     Moretti, Paul A. B.; Xia, Pu; Gamble, Jennifer R.;
     Vadas, Mathew A.; Wattenberg, Binks W. [Reprint author]
CS   Hanson Centre for Cancer Research, Division of Human Immunology, Institute
     of Medical and Veterinary Science, Frome Road, Adelaide, SA, 5000,
     Australia
SO   Biochemical Journal, (1 September, 2000) Vol. 350, No. 2, pp. 429-441.
     print.
     ISSN: 0264-6021.
DT   Article
LA   English
ED   Entered STN: 1 Nov 2000
     Last Updated on STN: 10 Jan 2002
AB   Sphingosine 1-phosphate (S1P) is a novel lipid
     messenger that has important roles in a wide variety of mammalian
     cellular processes including growth, differentiation and death.
     Basal levels of S1P in mammalian cells are generally low, but
     can increase rapidly and transiently when cells are exposed to
     mitogenic agents and other stimuli.  This increase is largely due to
     increased activity of sphingosine kinase (SK), the enzyme that
     catalyses its formation.  In the current study we have purified, cloned
     and characterized the first human SK to obtain a better understanding of
     its biochemical activity and possible activation mechanisms.  The enzyme
     was purified to homogeneity from human placenta using ammonium sulphate
     precipitation, anion-exchange chromatography, calmodulin-affinity
     chromatography and gel-filtration chromatography.  This resulted in a
     purification of over 106-fold from the original placenta extract.  The
     enzyme was cloned and expressed in active form in both HEK-293T
```

cells and Escherichia coli, and the recombinant E. coli-derived SK purified to homogeneity. To establish whether post-translational modifications lead to activation of human SK activity we characterized both the purified placental enzyme and the purified recombinant SK produced in E. coli, where such modifications would not occur. The premise for this study was that post-translational modifications are likely to cause conformational changes in the structure of SK, which may result in detectable changes in the physico-chemical or catalytic properties of the enzyme. Thus the enzymes were characterized with respect to substrate specificity and kinetics, inhibition kinetics and various other physico-chemical properties. In all cases, both the native and recombinant SKs displayed **remarkably** similar properties, indicating that post-translational modifications are not required for basal activity of human SK.

CC Physiology and biochemistry of bacteria 31000
Cytology - Human 02508
Enzymes - General and comparative studies: coenzymes 10802

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics)

IT Chemicals & Biochemicals
recombinant **sphingosine** kinase; **sphingosine** 1-phosphate; **sphingosine** kinase: posttranslational modification

IT Methods & Equipment
ammonium sulfate precipitation: purification method; anion-exchange chromatography: purification method; calmodulin-affinity chromatography: purification method; gel-filtration chromatography: purification method

IT Miscellaneous Descriptors
interspecific amino acid sequence comparison

ORGN Classifier
Enterobacteriaceae 06702
Super Taxa
Facultatively Anaerobic Gram-Negative Rods; Eubacteria; Bacteria; Microorganisms
Organism Name
Escherichia coli
Taxa Notes
Bacteria, Eubacteria, Microorganisms

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
293 **cell** line
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 26993-30-6 (**sphingosine** 1-phosphate)
50864-48-7 (**sphingosine** kinase)

L80 ANSWER 7 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2000:70577 BIOSIS
DN PREV200000070577
TI Activation of **sphingosine** kinase by tumor necrosis factor-alpha inhibits apoptosis in human endothelial **cells.**
AU **Xia, Pu**; Wang, Lijun; **Gamble, Jennifer R.**; **Vadas, Mathew A.** [Reprint author]
CS Division of Human Immunology, The Hanson Centre for Cancer Research, Institute of Medical and Veterinary Science and University of Adelaide, Adelaide, South Australia, Australia
SO Journal of Biological Chemistry, (Nov. 26, 1999) Vol. 274, No. 48, pp. 34499-34505. print.
CODEN: JBCHA3. ISSN: 0021-9258.
DT Article
LA English

ED Entered STN: 16 Feb 2000
Last Updated on STN: 3 Jan 2002

AB Human umbilical vein endothelial **cells** (HUVEC), like most normal **cells**, are resistant to tumor necrosis factor-alpha (TNF)-induced apoptosis in spite of TNF activating sphingomyelinase and generating ceramide, a known inducer of apoptosis. Here we report that TNF activates another key enzyme, **sphingosine** kinase (SphK), in the sphingomyelin metabolic pathway resulting in production of **sphingosine**-1-phosphate (S1P) and that S1P is a potent antagonist of TNF-mediated apoptosis. The TNF-induced SphK activation is independent of sphingomyelinase and ceramidase activities, suggesting that TNF affects this enzyme directly other than through a mass effect on sphingomyelin degradation. In contrast to normal HUVEC, in a spontaneously transformed endothelial **cell** line (C11) TNF stimulation failed to activate SphK and induced apoptosis as characterized by morphological and biochemical criteria. Addition of exogenous S1P or increasing endogenous S1P by phorbol ester **markedly** protected C11 **cell** line from TNF-induced apoptosis. Conversely, N,N-**dimethylsphingosine** , an inhibitor of SphK, profoundly sensitized normal HUVEC to killing by TNF. Thus, we demonstrate that the activation of SphK by TNF is an important signaling for protection from the apoptotic effect of TNF in endothelial **cells.**

CC Enzymes - General and comparative studies: coenzymes 10802
Biochemistry methods - General 10050
Biochemistry studies - General 10060

IT Major Concepts
Enzymology (Biochemistry and Molecular Biophysics)

IT Parts, Structures, & Systems of Organisms
endothelial **cells**

IT Chemicals & Biochemicals
sphingosine kinase: activation; tumor necrosis factor-alpha

IT Miscellaneous Descriptors
apoptosis; enzyme activity

ORGN Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
HUVEC **cell** line
human
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 50864-48-7 (**sphingosine** kinase)

L80 ANSWER 8 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1991:428265 BIOSIS
DN PREV199192084430; BA92:84430
TI HEPATIC LIPASE PROMOTES A LOSS OF APOLIPOPROTEIN A-I FROM TRIGLYCERIDE-ENRICHED HUMAN HIGH DENSITY LIPOPROTEINS DURING INCUBATION IN-VITRO.
AU CLAY M A [Reprint author]; NEWNHAM H H; **BARTER P J**
CS GRADUATE SCH HEALTH MED SCI, UNIV WOLLONGONG, PO BOX 1144, WOLLONGONG, NEW SOUTH WALES, 2500 AUST
SO Arteriosclerosis and Thrombosis, (1991) Vol. 11, No. 2, pp. 415-422.
CODEN: ARTTE5. ISSN: 1049-8834.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 26 Sep 1991
Last Updated on STN: 26 Sep 1991

AB Studies have been performed to investigate a possible mechanism to account for the low concentrations of apolipoprotein A-I (apo A-I) in subjects with hypertriglyceridemia. Incubation of human plasma in vitro with canine hepatic lipase resulted in the hydrolysis of approximately half the triglyceride in the high density lipoproteins (HDLs), but little change in the concentratins of other HDL constituents. However, when the plasma was

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     supplemented with cholesteryl ester transfer protein and very low density
     lipoproteins to enrich the HDL with triglyceride, hepatic lipase promoted
     not only a significant reduction if HDL triglyceride acquired by the
     lipid transfer process but also an enhanced transfer of
     cholesteryl esters out of the particles.  These changes were accompanied
     by a marked loss of apo A-I from HDL, which was demonstrated
     independently by ultracetrifugation, size-exclusion chromatography, and
     gradient gel-immunoblot analysis.  The apo A-I lost from HDL was recovered
     in the "lipoprotein-free" fraction of plasma.  The results of these
     studies indicate that primary reductions in the concentration of HDL core
     lipids in vitro are accompanied by a secondary loss of apo A-I
     fron HDL.  While recognizing the need for caution in any extrapolation
     from observations made in vitro to what may occur in vivo, these studies
     are nevertheless consistent with a proposition that the low concentration
     of apo A-I in subjects with hypertriglyceridemia is secondary to the
     reduced concentration of HDL core lipids in such subjects.
CC   Cytology - Human   02508
     Biochemistry methods - Proteins, peptides and amino acids   10054
     Biochemistry methods - Lipids   10056
     Biochemistry studies - Proteins, peptides and amino acids   10064
     Biochemistry studies - Lipids   10066
     Biophysics - Methods and techniques   10504
     Biophysics - Membrane phenomena   10508
     Enzymes - Chemical and physical   10806
     Enzymes - Physiological studies   10808
     Movement   12100
     Metabolism - Lipids   13006
     Metabolism - Proteins, peptides and amino acids   13012
     Metabolism - Metabolic disorders   13020
     Digestive system - General and methods   14001
     Cardiovascular system - Physiology and biochemistry   14504
     Cardiovascular system - Blood vessel pathology   14508
     In vitro cellular and subcellular studies   32600
     Immunology - General and methods   34502
IT   Major Concepts
        Biochemistry and Molecular Biophysics; Cardiovascular Medicine (Human
        Medicine, Medical Sciences); Cardiovascular System (Transport and
        Circulation); Cell Biology; Enzymology (Biochemistry and
        Molecular Biophysics); Membranes (Cell Biology); Metabolism
IT   Miscellaneous Descriptors
        CANINE CHOLESTERYL ESTER TRANSFER PROTEIN HYPERTRIGLYCERIDEMIA
        ULTRACENTRIFUGATION SIZE-EXCLUSION CHROMATOGRAPHY GRADIENT
        GEL-IMMUNOBLOT ANALYSIS
ORGN Classifier
        Hominidae   86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN   9001-62-1 (LIPASE)
     20910-06-9D (CHOLESTERYL)

L80  ANSWER 9 OF 12  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
AN   1990:422180  BIOSIS
DN   PREV199090082981; BA90:82981
TI   GLYCOLIPID AND GLYCOPROTEIN TRANSPORT THROUGH THE GOLGI COMPLEX
     ARE SIMILAR BIOCHEMICALLY AND KINETICALLY RECONSTITUTION OF
     GLYCOLIPID TRANSPORT IN A CELL FREE SYSTEM.
AU   WATTENBERG B W [Reprint author]
CS   CELL BIOLOGY UNIT, UPJOHN COMPANY, KALAMAZOO, MICH 49007, USA
SO   Journal of Cell Biology, (1990) Vol. 111, No. 2, pp. 421-428.
     CODEN: JCLBA3. ISSN: 0021-9525.
DT   Article
FS   BA
LA   ENGLISH
ED   Entered STN: 22 Sep 1990
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Last Updated on STN: 23 Sep 1990

AB **Glycolipid** transport between compartments of the Golgi apparatus has been reconstituted in a **cell** free system. Transport of lactosylceramide (galactose β1-4-glucose-ceramide) was followed from a donor to an acceptor Golgi population. The major **glycolipid** in CHO **cells** is GM3 (sialic acid α2-3 galactose β1-4-glucose-ceramide). Donor membranes were derived from a Chinese hamster ovary (CHO) **cell** mutant (Lec2) deficient in the Golgi CMP-sialic acid transporter, and therefore contained lactosylceramide as the predominant **glycolipid.** Acceptor Golgi apparatus was prepared from another mutant, Lec8, which is defective in UDP-Gal transport. Thus, glucosylceramide is the major **glycolipid** in Lec8 **cells.** Transport was measured by the incorporation of **labeled** sialic acid into lactosylceramide (present originally in the donor) by transport to acceptor membranes, forming GM3. This incorporation was dependent on ATP, cytosolic components, intact membranes, and elevated temperature. Donor membranes were prepared from Lec2 **cells** infected with vesicular stomatitis virus (VSV). These membranes therefore contain the VSV membrane glycoprotein, G protein. Donor membranes derived from VSV-infected **cells** could then be used to monitor both **glycolipid** and glycoprotein transport. Transport of these two types of molecules between Golgi compartments was compared biochemically and kinetically. **Glycolipid** transport required the N-ethylmaleimide sensitive factor previously shown to act in glycoprotein transport (Glick, B. S., and J. E. Rothman. 1987. Nature [Lond.]. 326:309-312; Rothman, J. E. 1987. J. Biol. Chemical 262:12502-12510). GTPγS inhibited **glycolipid** and glycoprotein transport similarly. The kinetics of transport of **glycolipid** and glycoprotein were also compared. The kinetics of transport to the end of the pathway were similar, as were the kinetics of movement into a defined transport intermediate. It is concluded that **glycolipid** and glycoprotein transport through the Golgi occur by similar if not identical mechanisms.

CC Cytology - Animal 02506
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Biophysics - Membrane phenomena 10508
Metabolism - Lipids 13006
Metabolism - Proteins, peptides and amino acids 13012

IT Major Concepts
Biochemistry and Molecular Biophysics; **Cell** Biology; Membranes (**Cell** Biology); Metabolism

IT Miscellaneous Descriptors
CHINESE HAMSTER OVARY LEC-8 **CELLS** LACTOSYLCERAMIDE N ETHYLMALEIMIDE ATP

ORGN Classifier
Cricetidae 86310
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates

RN 4682-48-8 (LACTOSYLCERAMIDE)
128-53-0 (N-ETHYLMALEIMIDE)
56-65-5Q (ATP)
42530-29-0Q (ATP)
94587-45-8Q (ATP)
111839-44-2Q (ATP)
87805-51-4Q (ATP)

L80 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 1990:285402 BIOSIS
DN PREV199090016248; BA90:16248
TI HUMAN TUMOR NECROSIS FACTOR-ALPHA TNF-ALPHA DIRECTLY STIMULATES

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     ARACHIDONIC ACID RELEASE IN HUMAN NEUTROPHILS.
AU   ATKINSON Y H [Reprint author]; MURRAY A W; KRILIS S; VADAS M A;
     LOPEZ A F
CS   DIV HUMAN IMMUNOL, INST VET SCI, ADELAIDE, SOUTH AUSTRALIA
SO   Immunology, (1990) Vol. 70, No. 1, pp. 82-87.
     CODEN: IMMUAM. ISSN: 0019-2805.
DT   Article
FS   BA
LA   ENGLISH
ED   Entered STN: 23 Jun 1990
     Last Updated on STN: 24 Jun 1990
AB   The ability of tumour necrosis factor-alpha (TNF-α) to directly
     stimulate phospholipid turnover from human neutrophils was
     studied.  Stimulation with recombinant human (rH)TNF-α induced the
     release of significant amounts of radioactivity from [3H]arachidonic acid-
     labeled neutrophils.  This stimulation was equipotent to that
     induced by the bacterial tripeptide formyl-methionyl-leucyl-phenylalanine
     (FMLP).  The time of maximum stimulated release varied between donors,
     with the most common maximal stimulation being 45 min.  Dose-response
     experiments indicated that 100-1000 U/ml rH TNF-α were required for
     the maximum stimulatory effect.  High-performance liquid chromatography
     analysis of the supernatants revealed that the radioactivity was
     associated with arachidonic acid, but not with its metabolites, indicating
     that TNF-α stimulates the release of arachidonic acid from
     cellular phospholipids but does not stimulate its
     metabolism.  A comparison of TNF-α with other cytokines indicated
     that stimulation of arachidonic acid release paralleled the 'priming' of
     neutrophils for enhanced superoxide production, raising the possibility
     that phospholipid turnover and priming of neutrophils are
     causally related.
CC   Cytology - Human   02508
     Biochemistry studies - Proteins, peptides and amino acids   10064
     Biochemistry studies - Lipids   10066
     Biophysics - Methods and techniques   10504
     Blood - Blood cell studies   15004
     Blood - Lymphatic tissue and reticuloendothelial system   15008
     Endocrine - General   17002
     Immunology - Immunopathology, tissue immunology   34508
IT   Major Concepts
        Blood and Lymphatics (Transport and Circulation); Clinical
        Endocrinology (Human Medicine, Medical Sciences); Endocrine System
        (Chemical Coordination and Homeostasis)
IT   Miscellaneous Descriptors
          PHOSPHOLIPID HIGH PERFORMANCE LIQUID CHROMATOGRAPHY
ORGN Classifier
        Hominidae   86215
     Super Taxa
        Primates; Mammalia; Vertebrata; Chordata; Animalia
     Taxa Notes
        Animals, Chordates, Humans, Mammals, Primates, Vertebrates
RN   506-32-1 (ARACHIDONIC ACID)

L80  ANSWER 11 OF 12  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on
     STN
AN   1985:259675  BIOSIS
DN   PREV198579039671; BA79:39671
TI   A TRANSIENT INCREASE IN DIACYLGLYCEROLS IS ASSOCIATED WITH THE ACTION OF
     VASOPRESSIN ON HEPATOCYTES.
AU   HUGHES B P [Reprint author]; RYE K-A; PICKFORD L B; BARRITT G J;
     CHALMERS A H
CS   DEP OF CLINICAL BIOCHEM, FLINDERS UNIV SCH OF MED, FLINDERS MED CENT,
     BEDFORD PARK, SOUTH AUSTRALIA 5042, AUSTRALIA
SO   Biochemical Journal, (1984) Vol. 222, No. 2, pp. 535-540.
     ISSN: 0264-6021.
DT   Article
FS   BA
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LA    ENGLISH
AB    Vasopressin induced a transient increase of 50% in the total concentration
      of diacylglycerols in isolated hepatocytes.  The increase was maximal at
      0.25 min, and the concentration of diacylglycerols in cells
      treated with vasopressin had returned to the basal value by 4 min.  No
      change in the concentration of diacylglycerols was observed after the
      treatment of cells with glucagon.  The dependency of this effect
      on the concentration of vasopressin was similar to that of the effect of
      the hormone on 45Ca2+ efflux measured at 0.1 mM extracellular Ca2+.
      Vasopressin increased the proportion of arachidonic acid and stearic acid
      and decreased the proportion of oleic acid present in the diacylglycerols.
      In hepatocytes prelabeled with [14C]arachidonic acid,
      vasopressin increased the amount of [14C]diacylglycerol.  The effects of
      vasopressin on the total concentration of diacylglycerols and
      [14C]diacylglycerol were mimicked by an exogenous phospholipid
      phosphodiesterase (phospholipase C) from Clostridium perfringens.  The
      transient increase in diacylglycerols induced could be caused by the rapid
      hydrolysis of both the phosphoinositides and 1 or more other
      phospholipids.
CC    Cytology - Animal   02506
      Comparative biochemistry   10010
      Biochemistry methods - Lipids   10056
      Biochemistry studies - General   10060
      Biochemistry studies - Proteins, peptides and amino acids   10064
      Biochemistry studies - Lipids   10066
      Biochemistry studies - Minerals   10069
      Biophysics - Molecular properties and macromolecules   10506
      Enzymes - Methods   10804
      Enzymes - Physiological studies   10808
      Metabolism - General metabolism and metabolic pathways   13002
      Metabolism - Lipids   13006
      Metabolism - Minerals   13010
      Digestive system - Physiology and biochemistry   14004
      Endocrine - Pancreas   17008
      Endocrine - Pituitary   17014
      Endocrine - Neuroendocrinology   17020
      Nervous system - Physiology and biochemistry   20504
      Pharmacology - Drug metabolism and metabolic stimulators   22003
      Pharmacology - Endocrine system   22016
      Physiology and biochemistry of bacteria   31000
IT    Major Concepts
         Biochemistry and Molecular Biophysics; Cell Biology;
         Digestive System (Ingestion and Assimilation); Endocrine System
         (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and
         Molecular Biophysics); Metabolism; Pharmacology
IT    Miscellaneous Descriptors
         CLOSTRIDIUM-PERFRINGENS PHOSPHOLIPASE-C PHOSPHOLIPID
         PHOSPHODIESTERASE GLUCAGON PHOSPHOINOSITIDE HYDROLYSIS CALCIUM-II
         EFFLUX ARACHIDONIC-ACID STEARIC-ACID OLEIC-ACID
ORGN  Classifier
         Endospore-forming Gram-Positives   07810
      Super Taxa
         Eubacteria; Bacteria; Microorganisms
      Taxa Notes
         Bacteria, Eubacteria, Microorganisms
RN    11000-17-2 (VASOPRESSIN)
      9001-86-9Q (PHOSPHOLIPASE-C)
      63551-76-8Q (PHOSPHOLIPASE-C)
      9025-82-5 (PHOSPHODIESTERASE)
      9007-92-5 (GLUCAGON)
      14127-61-8 (CALCIUM-(II))
      506-32-1 (ARACHIDONIC-ACID)
      57-11-4 (STEARIC-ACID)
      112-80-1 (OLEIC-ACID)

L80   ANSWER 12 OF 12  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on
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STN
AN 1980:201672 BIOSIS
DN PREV198069076668; BA69:76668
TI DIFFERENCES IN THE METABOLISM OF VERY LOW DENSITY LIPO PROTEINS BY ISOLATED BEATING HEART **CELLS** AND THE ISOLATED PERFUSED RAT HEART EVIDENCE FOR COLLAGENASE RELEASED EXTRACELLULAR LIPO PROTEIN LIPASE.
AU RAJARAM O V [Reprint author]; CLARK M G; **BARTER P J**
CS CLIN BIOCHEM UNIT, SCH MED, FLINDERS UNIV, BEDFORD PARK, S AUST 5042, AUST
SO Biochemical Journal, (1980) Vol. 186, No. 2, pp. 431-438.
ISSN: 0264-6021.
DT Article
FS BA
LA ENGLISH

AB The metabolism of VLD lipoproteins (very-low-density lipoproteins) was studied in intact isolated beating-heart **cells** and isolated perfused rat heart from starved animals by using [14C]triacylglycerol **fatty acid-labelled** VLD lipoprotein prepared from rats previously injected with [1-14C]palmitate. 14C-**labelled** VLD lipoprotein was metabolized by the isolated perfused heart, but was only minimally metabolized by the heart **cells** unless an exogenous source of lipoprotein lipase was added. Measurements of lipoprotein lipase at pH 7.4 with the natural substrate 14C-**labelled** VLD lipoprotein indicated that during collagenase perfusion of the heart the enzyme was released into the perfusate, the activity released being proportional to the concentration of collagenase used. Lipoprotein lipase activity in homogenates of hearts that were perfused with collagenase showed a corresponding loss of activity. At high perfusate concentrations of collagenase, inactivation of the released lipoprotein lipase occurred. Lipoprotein lipase activity was largely undetectable in the homogenate of the isolated heart **cells**. The lipoprotein lipase responsible for the hydrolysis of VLD lipoprotein triacylglycerol is predominantly located externally to the heart muscle **cells** and its release can be facilitated by perfusion of the heart with bacterial collagenase.

CC Cytology - Animal 02506
Radiation biology - Radiation and isotope techniques 06504
Biochemistry studies - General 10060
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Lipids 10066
Enzymes - Methods 10804
Enzymes - Physiological studies 10808
Metabolism - Lipids 13006
Metabolism - Proteins, peptides and amino acids 13012
Nutrition - Malnutrition and obesity 13203
Cardiovascular system - General and methods 14501
Cardiovascular system - Physiology and biochemistry 14504
Routes of immunization, infection and therapy 22100
Physiology and biochemistry of bacteria 31000
In vitro cellular and subcellular studies 32600
IT Major Concepts
Cardiovascular System (Transport and Circulation); **Cell** Biology; Enzymology (Biochemistry and Molecular Biophysics); Metabolism
IT Miscellaneous Descriptors
BACTERIAL COLLAGENASE
ORGN Classifier
Bacteria 05000
Super Taxa
Microorganisms
Taxa Notes
Bacteria, Eubacteria, Microorganisms
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals,

```
          Rodents, Vertebrates
RN     9001-12-1 (COLLAGENASE)
       9004-02-8 (LIPOPROTEIN LIPASE)
       83137-80-8Q (LIPO PROTEIN LIPASE)


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L126 ANSWER 1 OF 3  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN     2004-399250 [37]   WPIX
DNC    C2004-149456
TI     New diazinopyrimidine derivatives are protein kinase inhibitors, useful
       for treating e.g. arthritis and inflammatory bowel disease.
DC     B02
IN     CHEN, J J; LUK, K T; LUK, K
PA     (CHEN-I) CHEN J J; (LUKK-I) LUK K T; (HOFF) HOFFMANN LA ROCHE &
       CO AG F
CYC    107
PI     US 2004097493    A1 20040520 (200437)*      39    A61K031-549
       WO 2004046152    A1 20040603 (200437)  EN         C07D498-04
          RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE
              LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
           W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
              DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP
              KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NI NO NZ OM PG
              PH PL PT RO RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC
              VN YU ZA ZM ZW
       AU 2003283393    A1 20040615 (200470)             C07D498-04
ADT    US 2004097493 A1 Provisional US 2002-427652P 20021118, US 2003-715666
       20031118; WO 2004046152 A1 WO 2003-EP12652 20031112; AU 2003283393 A1 AU
       2003-283393 20031112
FDT    AU 2003283393 A1 Based on WO 2004046152
PRAI   US 2002-427652P       20021118; US 2003-715666       20031118
IC     ICM  A61K031-549; C07D498-04
       ICS  A61K031-519; A61K031-53; A61K031-5395; A61P011-00; A61P019-02;
            A61P025-28; A61P029-00; A61P035-00; C07D487-02; C07D491-02;
            C07D498-02
```

AB US2004097493 A UPAB: 20040611

NOVELTY - Diazinopyrimidine derivatives (I) are new.

DETAILED DESCRIPTION - Diazinopyrimidine derivatives of formula (I), or their salts are new.

R1, R5 and R6 = H or alkyl;

R2 = (halo)alkyl, (hetero)aryl, (hetero)aralkyl, (cycloalkyl)alkyl, heteroalkyl substituted cycloalkyl, heterosubstituted cycloalkyl, heteroalkyl, cyanoalkyl, (heterocyclyl)alkyl or -Y1-C(O)-Y2-R11;

Y1 and Y2 = absent or alkylene;

R11 = T or haloalkyl;

T = H, alkyl, OH, alkoxy, amino, mono- or di-alkylamino;

R3 = H, (cyclo)alkyl, cycloalkylalkyl, heterosubstituted cycloalkyl, heterocyclyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, alkylene-C(O)-R4 or acyl;

R4 = T;

Ar1 = aryl;

X1 = O, NR5 or S;

X2 = bond, O, NR6, S or CH2.

INDEPENDENT CLAIMS are included for the following:

(a) preparation of (I); and

(b) a diazinopyrimidine derivative of formula (II).

n = 0 - 2;

R7 = alkyl.

ACTIVITY - Antiarthritic; Antiinflammatory; Gastrointestinal-Gen.; Respiratory-Gen.; Antiarteriosclerotic; Vasotropic; Cytostatic; Antirheumatic; Osteopathic; Dermatological; Immunosuppressive; Antiasthmatic; Antibacterial; Virucide; Antimalarial; Immunomodulator; Anti-HIV; CNS-Gen.; Cardiant; Thrombolytic; Nephrotropic; Neuroprotective; Antidiabetic; Antipsoriatic; Vulnerary; Antiulcer; Ophthalmological; Antiangiogenic; Gynecological.

MECHANISM OF ACTION - p38 **Mitogen-activated protein (MAP) kinase** inhibitor; Fibroblast growth factor receptor (FGFR) kinase inhibitor.

The p38 **MAP kinase** inhibitory activity of 2-methyl-4-(2-chlorophenyl)-6-(tetrahydropyranyl-4-amino)-4H-1,3,4-pyrimido(4,5-e)oxadiazone (Ia) in vitro was evaluated by measuring the transfer of the gamma -phosphate from gamma -33**P-ATP** by p-38 kinase to Myelin Basic Protein (MBP), using modified method as described in Ahn, N. G.; et al. J. Biol. Chemical Volume 266(7), 4220 - 4227, (1991). (Ia) Showed an IC50 value of 0.189 micro M.

USE - For treating p38 **MAP kinase** mediated disorder (e.g. arthritis, Crohn's disease, inflammatory bowel disease, adult respiratory distress syndrome and chronic obstructive pulmonary disease) and FGFR kinase mediated disorder (e.g. atherosclerosis, restenosis and cancer) (all claimed). Also useful for treating rheumatoid arthritis, spondyloarthropathies, gouty arthritis, osteoarthritis, systemic lupus erythematosus, juvenile arthritis, pulmonary disorders or lung inflammation (e.g. pulmonary sarcoidosis, asthma, silicosis and chronic pulmonary inflammatory disease), viral and bacterial infections (e.g. sepsis, septic shock, gram negative sepsis, malaria, meningitis, cachexia secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome (AIDS), AIDS, ARC (AIDS related complex), pneumonia and herpes virus), bone resorption diseases (e.g. osteoporosis, endotoxic shock, toxic shock syndrome, reperfusion injury, autoimmune disease (e.g. graft versus host reaction and allograft rejections), cardiovascular diseases (e.g. thrombosis, congestive heart failure and cardiac reperfusion injury), renal reperfusion injury, liver disease, nephritis and myalgias due to infection, influenza, multiple sclerosis, diabetes, systemic lupus erthrematosis (SLE), skin-related conditions (e.g. psoriasis, eczema, burns, dermatitis, keloid formation and scar tissue formation), gastrointestinal conditions (e.g. gastritis, irritable bowel disease and ulcerative colitis), ophthalmic diseases (e.g. retinitis, retinopathies, uveitis, ocular photophobia and of acute injury to the eye tissue), angiogenesis (e.g. neoplasia), metastasis, ophthalmological conditions (e.g. corneal graft rejection, ocular neovascularization, retinal neovascularization including

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     neovascularization following injury or infection, diabetic retinopathy,
     retrolental fibroplasia and neovascular glaucoma), ulcerative diseases
     (e.g. gastric ulcer), hemangiomas (e.g. infantile hemangiomas),
     angiofibroma of the nasopharynx and avascular necrosis of bone, diabetic
     nephropathy and cardiomyopathy; and disorders of the female reproductive
     system (e.g. endometriosis).
          ADVANTAGE - The compounds are inhibitors of protein kinases, and
     exhibit effective activity against p38 MAP kinase and
     FGFR kinase.
     Dwg.0/0
FS   CPI
FA   AB; GI; DCN
MC   CPI: B06-E03; B06-F03; B14-A01; B14-A02; B14-A03B; B14-D06; B14-E10;
          B14-F01; B14-F02; B14-F02D; B14-F02F2; B14-F04; B14-F07; B14-G01;
          B14-G02; B14-G03; B14-H01; B14-J01B3; B14-K01; B14-K01A; B14-N01;
          B14-N03; B14-N10; B14-N17; B14-S04

L126 ANSWER 2 OF 3  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2002-489654 [52]   WPIX
CR   2002-304240 [34]
DNC  C2002-138941
TI   New 7-oxo-pyridopyrimidines or their prodrugs or salts useful in the
     treatment of p38 mediated disorders e.g. arthritis.
DC   B02
IN   CHEN, J J; DUNN, J P; GOLDSTEIN, D M; LIM, J A; ARZENO, H B
PA   (HOFF) HOFFMANN LA ROCHE & CO AG F; (ARZE-I) ARZENO H B; (CHEN-I)
     CHEN J J; (DUNN-I) DUNN J P; (GOLD-I) GOLDSTEIN D M; (LIMJ-I) LIM
     J A; (SYNT) SYNTEX USA LLC
CYC  98
PI   WO 2002018379   A2 20020307 (200252)* EN   64    C07D471-04
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            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
            RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2002012147   A  20020313 (200252)             C07D471-04
     US 6506749      B2 20030114 (200313)             C07D471-04
     US 6518276      B2 20030211 (200314)             A61K031-519
     EP 1315727      A2 20030604 (200337)  EN         C07D471-04
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     KR 2003022423   A  20030315 (200350)             C07D471-04
     US 2003144307   A1 20030731 (200354)#            A61K031-519
     BR 2001013590   A  20030722 (200365)             C07D471-04
     CN 1451004      A  20031022 (200406)             C07D471-04
     MX 2003001733   A1 20030501 (200415)             A61K031-519
     JP 2004507540   W  20040311 (200419)      125    C07D471-04
     US 6753427      B2 20040622 (200445)             A61K031-519
     US 2004192709   A1 20040930 (200465)             A61K031-519
     ZA 2003001078   A  20040728 (200466)       78    C07D000-00
ADT  WO 2002018379 A2 WO 2001-EP9688 20010822; AU 2002012147 A AU 2002-12147
     20010822; US 6506749 B2 Provisional US 2000-229577P 20000831, Provisional
     US 2000-229584P 20000831, US 2001-943407 20010830; US 6518276 B2
     Provisional US 2000-229577P 20000831, Provisional US 2000-229584P
     20000831, US 2001-943338 20010830; EP 1315727 A2 EP 2001-980258 20010822,
     WO 2001-EP9688 20010822; KR 2003022423 A KR 2003-702955 20030227; US
     2003144307 A1 Div ex US 2001-943338 20010830, US 2002-315633 20021210; BR
     2001013590 A BR 2001-13590 20010822, WO 2001-EP9688 20010822; CN 1451004 A
     CN 2001-815027 20010822; MX 2003001733 A1 WO 2001-EP9688 20010822, MX
     2003-1733 20030226; JP 2004507540 W WO 2001-EP9688 20010822, JP
     2002-523894 20010822; US 6753427 B2 Provisional US 2000-229577P 20000831,
     Provisional US 2000-229584P 20000831, Div ex US 2001-943338 20010830, US
     2002-315633 20021210; US 2004192709 A1 Provisional US 2000-229577P
     20000831, Provisional US 2000-229584P 20000831, Div ex US 2001-943338
     20010830, Div ex US 2002-315633 20021210, US 2004-816554 20040401; ZA
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2003001078 A ZA 2003-1078 20030207

FDT AU 2002012147 A Based on WO 2002018379; EP 1315727 A2 Based on WO 2002018379; US 2003144307 A1 Div ex US 6518276; BR 2001013590 A Based on WO 2002018379; MX 2003001733 A1 Based on WO 2002018379; JP 2004507540 W Based on WO 2002018379; US 6753427 B2 Div ex US 6518276; US 2004192709 A1 Div ex US 6518276, Div ex US 6753427

PRAI	US 2000-229577P	20000831;	US 2000-229584P	20000831;
	US 2001-943407	20010830;	US 2001-943338	20010830;
	US 2002-315633	20021210;	US 2004-816554	20040401

IC ICM A61K031-519; C07D000-00; C07D471-04
ICS A61P001-04; A61P001-16; A61P003-10; A61P007-02; A61P009-04;
A61P009-10; A61P011-00; A61P011-06; A61P013-12; A61P015-08;
A61P019-02; A61P019-06; A61P019-10; A61P025-00; A61P025-28;
A61P027-02; A61P027-16; A61P029-00; A61P031-04; A61P031-06;
A61P031-16; A61P031-18; A61P031-22; A61P033-06; A61P035-00;
A61P035-04; A61P037-02; A61P037-06; C07D221-00; C07D239-00;
C07D239-46; C07D487-02

ICI C07D221:00; C07D239:00, C07D471-04; C07D221:00; C07D239:00; C07D471-04

AB WO 200218379 A UPAB: 20041015

NOVELTY - 7-Oxo-pyridopyrimidines (I) or their prodrugs or salts are new.

DETAILED DESCRIPTION - 7-Oxo-pyridopyrimidines of formula (I) or their salts or prodrugs are new.

R1 = H or alkyl;
R2 = -CR'R''-Ra, Rx-S(O)2-Ry, alkoxy-substituted alkyl, heterocyclylalkyl or 4-5C cycloalkyl;
R' and R'' = H, hydroxyalkyl or alkyl;
Ra = hydroxyalkyl;
Rx = alkyl;
Ry = alkenyl; or
N(R1R2) = heterocyclyl;
R3 = H, alkyl, amino, monoalkylamino, dialkylamino, cycloalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, alkylene-C(O)-R or acyl;
R = H, alkyl, hydroxy, alkoxy, amino, monoalkylamino or dialkylamino; and
Ar1 = aryl

with the proviso that the OH group in R2 can be in the form of an ester, carbamate, carbonate or a sulfonate derivative; and at least one of R' and R is alkyl or hydroxyalkyl.

INDEPENDENT CLAIMS are also included for:

(1) preparation of (I);

(2) preparation of pyrimidine compound of formula (IIc) comprising:

(a) contacting an acetal of formula NC-CH2-CH(ORa)2 with an alkyl formate of formula HCO2R in the presence of a condensation base to produce a condensed product; and

(b) contacting the condensed product with thiourea in the presence of a cyclization base to produce (IIc);

(3) preparation of pyridopyrimidine of formula (IIe) comprising either:

(i) contacting (IIc) with an alkylating agent of formula R-X1 in the presence of an alkylating base to produce alkylating pyrimidine of formula (IId); and

(ii) contacting (IId) with an aryl acetate of formula Ar1-CH2-CO2R (A) in the presence of a cyclization base to produce (IIe); or

(iii) contacting (IIc) with the aryl acetate of formula Ar1-CH2-CO2R in the presence of a cyclization base to produce a thiol pyridopyrimidine of formula (III); and

(iv) contacting (III) with the alkylating agent of formula R-X1 in the presence of alkylating base to produce to form (IIe);

(4) preparation of pyridopyrimidine of formula (Ie) comprising contacting (IIe) with a nitrogen alkylating agent of formula R3-X2;

(5) (IIc), (IIe) and (Ie); and

(6) use of (I) in the preparation of a medicament for the prevention or treatment of p38 mediated disorders.

R, Ra = alkyl;
X1 = leaving group;

R3' = alkyl, amino, mono- or di-alkylamino, cycloalkyl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, alkylene-C(O)-Rt or alkyl;

Rt = H, alkyl, hydroxy, alkoxy, anino or mono- or di-alkylamino;

X2 = leaving group.

ACTIVITY - Antiarthritic; Antiinflammatory; Nootropic; Neuroprotective; Antirheumatic; Antigout; Osteopathic; Dermatological; Immunosuppressive; Antiasthmatic; Antiviral; Antibacterial; Antiprotozoal; Antimalarial; Cerebroprotective; Immunomodulator; Anti-HIV; Vasotropic; Antiarteriosclerotic; Thrombolytic; Anticoagulant; Cardiant; Antidiabetic; Antipsoriatic; Vulnerary; Neuroleptic; Gastrointestinal; Antiulcer; Ophthalmological; Cytostatic; Nephrotropic; Gynecological; Cardiovascular; Respiratory; Antipyretic; Musculatropic; Antiallergic; Cholerectic; Analgesic; Endocrinal.

MECHANISM OF ACTION - p38 Mitogen-activated protein kinase (MAP) inhibitor; inhibitor of LPS-induced TNF- alpha production in THP1 cells; Antimetastatic; Protein kinase inhibitor; Cyclooxygenase-2 inhibitor.

The p-38 MAP kinase inhibitory activity of 6-(2-chloro-phenyl)-8-(4-fluoro-phenyl)-2-(2-hydroxy-1,2-dimethyl-propylamino)-8H-pyrido(2,3-d)pyrimidin-7-one (Ia) was determined by the transfer of the gamma -phosphate from gamma -33P-ATP by p-38 kinase to Myelin Basic Protein (MBP). (Ia) showed an IC50 of 0.0003 micro M.

USE - In the manufacture of a medicament useful in the treatment of p38 mediated disorders e.g. arthritis, Crohn's disease, Alzheimer's disease, irritable bowel syndrome, adult respiratory distress syndrome and chronic obstructive pulmonary disease; as a therapeutic agents (all claimed). As anti-inflammatory agent, as antipyretic; in the treatment of fever, rheumatoid arthritis, spondyloarthropathies, gouty arthritis, systemic lupus erythematosus, juvenile arthritis, osteoarthritis, other arthritic conditions; pulmonary disorders and lung inflammation, including pulmonary sarcoidosis, asthma, silicosis, chronic pulmonary inflammatory disease. In the treatment of viral and bacterial infections including sepsis, septic shock, gram negative sepsis, malaria, meningitis secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome (AIDS), ARC (AIDS related complex), pneumonia and herpes virus. Also in the treatment of bone resorption disease, osteoporosis, endotoxic shock, toxic shock syndrome, reperfusion injury disease including graft versus host reaction and allograft rejections, cardiovascular diseases including atherosclerosis, thrombosis, congestive heart failure, cardiac reperfusion injury, renal reperfusion injury, liver disease and nephritis, and myalgias due to infection; in the treatment of influenza, multiple sclerosis, cancer, diabetes, systemic lupus erythematosis, skin related conditions e.g. psoriasis, eczema, burns, dermatitis, keloid formation and scar tissue formation. In the treatment of gastrointestinal conditions such as inflammatory bowel disease and ulcerative colitis; ophthalmic diseases e.g. retinitis, retinopathies, uveitis, ocular photophobia, acute injury to the eye tissue, angiogenesis including neoplasia, metastasis; ophthalmological conditions e.g. corneal graft rejection, ocular neovascularization, retinal neovascularization including neovascularization following injury or infection, diabetic retinopathy, retrolental fibroplasia and neovascular glaucoma; ulcerative diseases e.g. gastric ulcer, pathological, but non-malignant conditions e.g. hemangiomas including infantile hemangiomas, angiofibroma of the nasopharynx and avascular necrosis of bone; diabetic nephropathy and cardiomyopathy; and disorders of the female reproductive system such as endometriosis. For preventing the production of cyclooxygenase-2; for veterinary treatment of companion animals, exotic animals and farm animals; in co-therapies. Also useful in the treatment of immunological, oncological, bronchopulmonary, dermatological and cardiovascular disease.

ADVANTAGE - (I) exhibits effective activity against p38 in vivo. (I) exhibits protein kinase inhibitory activity.

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: B06-D08; B06-H; B07-D12; B07-H; B11-C01C; B14-A01; B14-A01B2;
B14-A02; B14-A02A3; B14-A02B2; B14-A03B; B14-C02; B14-C03; B14-C04;
B14-C09; B14-C09A; B14-C09B; B14-D01B; B14-D05C; B14-D07C; B14-E08;

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       B14-E10; B14-E10C; B14-F01; B14-F01B; B14-F02; B14-F02F1; B14-F04;
       B14-F05; B14-F07; B14-G01B; B14-G02C; B14-G03; B14-H01; B14-H01B;
       B14-J01A2; B14-J01A4; B14-J05; B14-K01; B14-K01A; B14-K01F; B14-N01;
       B14-N03; B14-N10; B14-N12; B14-N14; B14-N16; B14-N17; B14-N17A;
       B14-N17B; B14-N17C; B14-S01; B14-S04; B14-S06; B14-S12

L126 ANSWER 3 OF 3  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2002-304240 [34]   WPIX
CR   2002-489654 [52]
DNC  C2002-088503
TI   New 7-oxo-pyridopyrimidine derivatives are p38 mitogen
     activated protein kinase inhibitors used for
     treating e.g. arthritis, Alzheimer's disease, bacterial infections and
     malaria.
DC   B02
IN   CHEN, J J; DUNN, J P; GOLDSTEIN, D M; LIM, J A; ARZENO, H B
PA   (HOFF) HOFFMANN LA ROCHE & CO AG F; (ARZE-I) ARZENO H B; (CHEN-I)
     CHEN J J; (DUNN-I) DUNN J P; (GOLD-I) GOLDSTEIN D M; (LIMJ-I) LIM
     J A; (SYNT) SYNTEX USA LLC
CYC  98
PI   WO 2002018380   A1 20020307 (200234)* EN  135    C07D471-04
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            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
            RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     US 2002055513   A1 20020509 (200235)             A61K031-519
     AU 2001093784   A  20020313 (200249)             C07D471-04
     US 2002137756   A1 20020926 (200265)             A61K031-519
     US 6506749      B2 20030114 (200313)             C07D471-04
     US 6518276      B2 20030211 (200314)             A61K031-519
     EP 1315726      A1 20030604 (200337)  EN         C07D471-04
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     KR 2003022422   A  20030315 (200350)             C07D471-04
     US 2003144307   A1 20030731 (200354)#            A61K031-519
     US 2003153586   A1 20030814 (200355)#            A61K031-519
     BR 2001013628   A  20030701 (200356)             C07D471-04
     CN 1451005      A  20031022 (200406)             C07D471-04
     MX 2003001821   A1 20030601 (200417)             A61K031-519
     JP 2004507541   W  20040311 (200419)      252    C07D471-04
     US 6753427      B2 20040622 (200445)             A61K031-519
     US 2004192709   A1 20040930 (200465)             A61K031-519
     ZA 2003001079   A  20040728 (200466)      138    C07D000-00
     US 6861423      B2 20050301 (200516)#            A61K031-535
ADT  WO 2002018380 A1 WO 2001-EP9689 20010822; US 2002055513 A1 Provisional US
     2000-229584P 20000831, US 2001-943338 20010830; AU 2001093784 A AU
     2001-93784 20010822; US 2002137756 A1 Provisional US 2000-229584P
     20000831, US 2001-943407 20010830; US 6506749 B2 Provisional US
     2000-229577P 20000831, Provisional US 2000-229584P 20000831, US
     2001-943407 20010830; US 6518276 B2 Provisional US 2000-229577P 20000831,
     Provisional US 2000-229584P 20000831, US 2001-943338 20010830; EP 1315726
     A1 EP 2001-974206 20010822, WO 2001-EP9689 20010822; KR 2003022422 A KR
     2003-702936 20030227; US 2003144307 A1 Div ex US 2001-943338 20010830, US
     2002-315633 20021210; US 2003153586 A1 Cont of US 2001-943407 20010830, US
     2002-230723 20020829; BR 2001013628 A BR 2001-13628 20010822, WO
     2001-EP9689 20010822; CN 1451005 A CN 2001-815030 20010822; MX 2003001821
     A1 WO 2001-EP9689 20010822, MX 2003-1821 20030228; JP 2004507541 W WO
     2001-EP9689 20010822, JP 2002-523895 20010822; US 6753427 B2 Provisional
     US 2000-229577P 20000831, Provisional US 2000-229584P 20000831, Div ex US
     2001-943338 20010830, US 2002-315633 20021210; US 2004192709 A1
     Provisional US 2000-229577P 20000831, Provisional US 2000-229584P
     20000831, Div ex US 2001-943338 20010830, Div ex US 2002-315633 20021210,
     US 2004-816554 20040401; ZA 2003001079 A ZA 2003-1079 20030207; US 6861423
     B2 Provisional US 2000-229577P 20000831, Provisional US 2000-229584P
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20000831, Cont of US 2001-943407 20010830, US 2002-230723 20020829

FDT AU 2001093784 A Based on WO 2002018380; EP 1315726 A1 Based on WO 2002018380; US 2003144307 A1 Div ex US 6518276; US 2003153586 A1 Cont of US 6506749; BR 2001013628 A Based on WO 2002018380; MX 2003001821 A1 Based on WO 2002018380; JP 2004507541 W Based on WO 2002018380; US 6753427 B2 Div ex US 6518276; US 2004192709 A1 Div ex US 6518276, Div ex US 6753427; US 6861423 B2 Cont of US 6506749

PRAI US 2000-229584P 20000831; US 2001-943338 20010830;
US 2001-943407 20010830; US 2000-229577P 20000831;
US 2002-315633 20021210; US 2002-230723 20020829;
US 2004-816554 20040401

IC ICM A61K031-519; A61K031-535; C07D000-00; C07D471-04
ICS A61K031-52; A61P001-04; A61P011-00; A61P011-06; A61P019-02; A61P025-28; A61P029-00; A61P031-00; A61P031-06; A61P037-06; A61P043-00; C07D221-00; C07D239-00; C07D487-02; C07D487-04

ICI C07D221:00; C07D239:00, C07D471-04; C07D221:00; C07D239:00; C07D471-04

AB WO 200218380 A UPAB: 20050316

NOVELTY - 7-Oxo-pyridopyrimidine derivatives (I) are new.

DETAILED DESCRIPTION - 7-Oxo-pyridopyrimidine derivatives of formula (I) and their salts and prodrugs are new.

R1 = H or alkyl;

R2 = substituted alkyl, optionally hetero substituted cycloalkyl, heteroalkyl substituted cycloalkyl, hetero substituted cycloalkyl-alkyl, heterocyclyl, heterocyclyl spirocycloalkyl, aralkoxy, alkoxy, -alkylene-S(O)n-alkyl or SO2Ar2;

n = 1 or 2;

R3 = H, amino, monoalkylamino, dialkylamino, acylamino, -NRa-C(=O)-Rb, alkyl, cycloalkyl, aryl, aralkyl, haloalkyl, heteroalkyl, cyanoalkyl, -alkylene-C(O)-R, acyl or phthalimidoalkyl;

Ra = H or alkyl;

Rb = heterocyclyl or heteroalkyl;

R = H, alkyl, hydroxy, alkoxy, amino, monoalkylamino or dialkylamino, and

Ar1, Ar2 = aryl.

An INDEPENDENT CLAIM is included for the preparation of (I).

ACTIVITY - Antiarthritic; Antiinflammatory; Nootropic; Neuroprotective; Antirheumatic; Antigout; Osteopathic; Dermatological; Immunosuppressive; Antiasthmatic; Virucide; Antibacterial; Protozoacide; Immunomodulator; Anti-HIV; Vasotropic; Antiarteriosclerotic; Thrombolytic; Anticoagulant; Cardiant; Antidiabetic; Dermatological; Antipsoriatic; Vulnerary; Neuroleptic; Gastrointestinal; Antiulcer; Ophthalmological; Cytostatic; Nephrotropic; Gynecological; Antipyretic.

MECHANISM OF ACTION - p38 **Mitogen-activated protein kinase** (**MAP**) inhibitor; LPS-induced tumor necrosis factor alpha (TNF- alpha) production inhibitor in THP1 cells; Cyclooxygenase-2 inhibitor.

In an assay measuring the transfer of the gamma -phosphate from gamma -**33P-ATP** by p-38 kinase to Myelin Basic Protein using a minor modification of the method described in Ahn, N. G; et al. J Biol. Chem Volume 266(7), 4220-4227, a compound of formula (Ia) exhibited an IC50 value of 3.00 multiply 10-10 M for inhibiting p38 enzyme.

USE - Used for treating arthritis, Crohn's disease, Alzheimer's disease, irritable bowel syndrome, adult respiratory distress syndrome and chronic obstructive pulmonary disease. (I) Are also used for treating fever, rheumatoid arthritis, spondyloarthropathies, gouty arthritis, systemic lupus erythematosus, juvenile arthritis, osteoarthritis, other arthritic conditions, pulmonary disorders and lung inflammation, including pulmonary sarcoidosis, asthma, silicosis, chronic pulmonary inflammatory disease, viral and bacterial infections including sepsis, septic shock, gram negative sepsis, malaria, meningitis secondary to infection or malignancy, cachexia secondary to acquired immune deficiency syndrome (AIDS), ARC (AIDS related complex), pneumonia and herpes virus.

(I) Are also used in the treatment of bone resorption disease, osteoporosis, endotoxic shock, toxic shock syndrome, reperfusion injury, autoimmune disease including graft versus host reaction and allograft rejections, cardiovascular diseases including atherosclerosis, thrombosis,

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          congestive heart failure, cardiac reperfusion injury, renal reperfusion
          injury, liver disease and nephritis, myalgias due to infection, influenza,
          multiple sclerosis, cancer, diabetes, systemic lupus erythematosis, skin
          related conditions e.g. psoriasis, eczema, burns, dermatitis, keloid
          formation and scar tissue formation, gastrointestinal conditions such as
          inflammatory bowel disease, gastritis and ulcerative colitis, ophthalmic
          diseases e.g. retinitis, retinopathies, uveitis, ocular photophobia, acute
          injury to the eye tissue, angiogenesis including neoplasia, metastasis,
          ophthalmological conditions e.g. corneal graft rejection, ocular
          neovascularization, retinal neovascularization including
          neovascularization following injury or infection, diabetic retinopathy,
          retrolental fibroplasia and neovascular glaucoma, ulcerative diseases e.g.
          gastric ulcer, pathological, but non-malignant conditions e.g. hemangiomas
          including infantile hemangiomas, angiofibroma of the nasopharynx and a
          vascular necrosis of bone, diabetic nephropathy and cardiomyopathy, and
          disorders of the female reproductive system such as endometriosis.
               (I) Are used for veterinary treatment of companion animals, exotic
          animals and farm animals.
          Dwg.0/0
FS        CPI
FA        AB; GI; DCN
MC        CPI: B06-D08; B14-A01; B14-A02; B14-A02A3; B14-A03B; B14-C03; B14-C04;
               B14-C09; B14-E08; B14-E10; B14-E10C; B14-F01B; B14-F04; B14-F05;
               B14-F07; B14-G01; B14-G01B; B14-H01; B14-J01A2; B14-J01A4; B14-K01;
               B14-K01A; B14-N01; B14-N03; B14-N10; B14-N12; B14-N14; B14-N16;
               B14-N17A; B14-N17B; B14-N17C; B14-S01; B14-S04; B14-S06


=> d all l123 tot


L123 ANSWER 1 OF 8  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN    1992-006838 [01]   WPIX
DNN   N1992-005295        DNC C1992-002905
TI    Very sensitive detection of cpds. partic. nucleotide(s) and proteins - is
      by binding to element forming radioactive isotope on neutron absorption.
DC    B04 D16 J04 K08 S03 S05
IN    BERNARD, J A; HARLING, O R; KWOK, K S; SNAPKA, R M; VARSHAVSKY, A
PA    (MASI) MASSACHUSETTS INST TECHNOLOGY
CYC   1
PI    US 5071775       A  19911210 (199201)*                          <--
ADT   US 5071775 A US 1986-896149 19860813
PRAI  US 1986-896149         19860813
IC    C12Q001-68; G01N033-53
AB    US    5071775 A UPAB: 19931006
      A method for detecting an organic molecular species of interest (OMSI) in
      a substrate compsn. comprises: (a) separating the compsn., using a support
      material or support matrix formed of elements which, when irradiated, have
      a half life less than both phosphorus and an element (ELNAC) having a
      large neutron absorption cross-section to isolate the OMSI; (b) binding
      the ELNAC (which is neutron-activatable to form a radioactive isotope) to
      the OMSI; (the separating step can be either prior to or subsequent to the
      binding step); (c) activating the ELNAC with neutrons to form a
      radioactive isotope (RI) and (d) detecting the presence of the OMSI by
      detecting the radiation emitted by the RI.
           USE/ADVANTAGE - Indirect labelling, is a very sensitive detection of
      OMSI after separation, via neutron activation, having an operational range down
      to attomole (10 power (-18) mole) level. Suitable OMSI are antigens,
      antibodies, enzymes and other proteins, nucleic acids, lipids,
      polysaccharides, polymers of non-biological origin, and low M.weight cpds.
      for which selectively binding activatable ligands can be designed. The
      detection sensitivities possible vastly exceed those available with prior
      art direct labelling (e.g. using 32P), since ELNAC are used which are
      highly activatable and more easily detectable.
      0/0
FS    CPI EPI
```

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FA   AB; DCN
MC   CPI: B04-B01B; B04-B02C; B04-B03B; B04-B04C; B04-C02; B04-C03;
          B05-A03; B11-C07A3; B11-C07B5; B12-K04; D05-H09; J04-B01;
          K08-B; K09-B; K09-E
     EPI: S03-E06D; S03-E14H9; S03-G02B9; S05-C09

L123 ANSWER 2 OF 8  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   1989-284608 [39]   WPIX
DNN  N1989-217208        DNC C1989-126169
TI   Monoclonal antibody reactive with tumour related fucoganglioside - useful
     for diagnosis, imaging and therapy of cancers, and new hybridomas.
DC   B04 D16 S03
IN   FUKUSHI, Y; HAKOMORI, S; LEVERY, S B; NUDELMAN, E D
PA   (HUTC-N) HUTCHINSON F CANCER
CYC  1
PI   US 4851511       A  19890725 (198939)*      17                   <--
ADT  US 4851511 A US 1986-824172 19860130
PRAI US 1986-824172        19860130
IC   A61K039-00; A61K043-00; C07K015-00; C12N005-00; G01N053-00
AB   US    4851511 A UPAB: 19930923
     Monoclonal antibodies (MAb) which specifically bind to the
     fucogangliosides disialosyl Le a and monosialosyl Lea II (i.e. IV (3)
     NeuAc III (6) New Ac III (4) Fuc Lc4 and (III) (6) New Ac III (4) FuC Lc4,
     respectively) are new.  Also new are (a) hybridoma cell lines which
     produce MAb and (b) diagnostic kits containing MAb for assaying presence of
     disialosyl Le a.
          MAb, especially of class IgG3, can be coupled to a radionucleotide,
     antitumour drug or label (e.g. enzyme, chromphone or fluorophone). The
     hybridoma ATCC H8 8861 is specifically claimed.
          USE/ADVANTAGE - Didialosyl Le a is a strongly immunogenic, human
     cancer-associated fucoganglioside, closely associated with malignancy.
     MAb can be used to detect it in many cancers (especially colorectal,
     gastrointestinal and pancreatic cancers in their early stages) and to
     monitor it during a course of treatment. When appropriate agents are
     coupled to MAb, they can also be used for tumour imaging and
     therapeutically.
     0/6
FS   CPI EPI
FA   AB; DCN
MC   CPI: B04-B01B; B04-B02C; B04-B04A3; B04-B04C4; B04-B04C5;
          B05-A04; B11-C07A; B12-G07; B12-K04A1; D05-A01A4; D05-A01B;
          D05-H08; D05-H09; D05-H11
     EPI: S03-E14H4

L123 ANSWER 3 OF 8  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   1989-093242 [12]   WPIX
DNN  N1989-070989        DNC C1989-041369
TI   Determn. of viral associated antigen or corresp. antibody - especially useful
     for diagnosis of Herpes virus infections.
DC   B04 J04 S03
IN   BREWER, J H; FOSTER, T L
PA   (FAIR-N) FAIRLEIGH DICKINSON
CYC  1
PI   US 4810629       A  19890307 (198912)*      12                   <--
ADT  US 4810629 A US 1985-780628 19850926
PRAI US 1980-170143        19800718; US 1981-323762        19811123;
     US 1983-493413        19830510; US 1984-645665        19840830;
     US 1985-780628        19850926
IC   G01N033-54
AB   US    4810629 A UPAB: 19930923
     The presence or absence of a viral antigen (Ag) or an antibody (Ab)
     specific for Ag in a biological fluid may be determined by mixing an
     extra-corporeal specimen of the biological fluid with an aqueous dispersion of
     solid, porous carrier particles with a complex of forula A x-y (I)
     adsorbed on them. Where X = a hydrophylic polar moiety; Y = a hydrophobic
     non-polar moiety; A = the immunological binding partner of Ag or Ab; X-Y
     is a phospholipid surfactant cpd. and the X-Y cpd is complexed with A such
     that the X moiety is oriented toward the polar A moiety and the Y moiety
     is oriented away from the polar A moiety and towards the particle. After
     mixing, a positive agglutination reaction is indicative of the  presence
     of the Ag or Ab and absence of agglutination reaction is indicative of the
     absence of Ag or Ab.
          Pref. determn. of the presence of Ag in a biological cell culture, is
     claimed. In this case, an aqueous dispersion of charcoal particles with a
     surfactant X-Y (i) and antibody (Ab), immunoreactive with Ag, adsorbed on
     them, is used for the agglutination reaction.
          USE/ADVANTAGE - The method is especially useful in the diagnosis and
     treatment of sexually transmitted viral infections, such as herpes virus
     infections. The process is economical, highly accurate, rapid and easily
     carried out with a minimum of training and practice. Expensive laboratory
     facilities are not required. The method also requires only small
     biological fluid samples for testing (less than 0.5 ml), providing the
     patient with less discomfort and loss of time. The process may be
     automated.
     1/1
FS   CPI EPI
FA   AB; GI
MC   CPI: B04-B01B; B04-B02B4; B04-B04C; B04-B04D5; B05-B01P;
          B05-C06; B11-C07A; B12-K04A4; J04-B01
     EPI: S03-E14H4

L123 ANSWER 4 OF 8  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   1987-349712 [50]   WPIX
DNN  N1987-262174       DNC C1987-149349
TI   Determining turnover of organic material in living tissue - by
     artificially modifying the deuterium content and monitoring by NMR
     spectroscopy.
DC   B04 C03 J04 K08 P31 S03
IN   IRVING, M
PA   (BRUK-N) BRUKER ANALYTISCHE MESSTECHNIK
CYC  12
PI   EP 248924        A  19871216 (198750)* EN     7
         R: AT BE CH DE FR GB IT LI LU NL SE
     EP 248924        B  19891123 (198947)  EN
         R: DE FR GB NL
     DE 3667103       G  19891228 (199002)
     US 4889126       A  19891226 (199008)         7                <--
ADT  EP 248924 A EP 1986-107834 19860609; US 4889126 A US 1987-58302 19870605
PRAI EP 1986-107834       19860609
REP  8.Jnl.Ref; 9.Jnl.Ref
IC   A61B005-04; A61K049-00; G01N024-08
AB   EP    248924 A UPAB: 19930922
     A method for determining the turnover of organic material stored in living
     tissue is characterised in that the deuterium content of the stored
     material is artificially modified from natural abundance and monitored as
     a function of time by measuring the CHD-signal by magnetic resonance
     spectroscopy. For artificially modifying the deuterium content of the
     stored material, the living tissue can be supplied with water containing heavy
     water in a proportion which is different from natural abundance.
          USE/ADVANTAGE - The method can be used in various fields e.g.
     biological research on plants and animals, agriculture and stock farming,
     quality control of farming prods. etc. The method is non-invasive and
     allows investigation of narrow body regions.
     0/3
FS   CPI EPI GMPI
FA   AB; DCN
MC   CPI: B04-B01B; B04-B04A6; B05-A04; B11-C08A;
          B12-K04A; B12-K04D; B12-K04E; C04-B01B; C04-B04A6;
          C05-A04; C11-C08A; C12-K04A; C12-K04D; C12-K04E;
          J04-B01A; J04-C04; K09-B; K09-E
     EPI: S03-E07
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L123 ANSWER 5 OF 8  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   1986-225518 [34]   WPIX
DNN  N1986-168273       DNC C1986-097327
TI   Reagent for determining analyte in lipid vesicle immunoassay - comprises
     glucose 6-phosphate dehydrogenase encapsulated in oligo lamellar lipid
     vesicles.
DC   B04 D16 S03
IN   CANOVDAVI, E; KUNG, V; REDEMANN, C T
PA   (COOP-N) COOPER-LIPOTECH INC
CYC  13
PI   WO 8604682      A  19860814 (198634)* EN   55
        RW: AT BE CH DE FR GB IT LU NL SE
         W: JP
     US 4622294      A  19861111 (198648)                        <--
     EP 215027       A  19870325 (198712)  EN
         R: AT BE CH DE FR GB IT LI LU NL SE
     JP 62501800     W  19870716 (198734)
ADT  WO 8604682 A WO 1986-US279 19860207; US 4622294 A US 1985-699860 19850208;
     EP 215027 A EP 1986-901277 19860207; JP 62501800 W JP 1986-501117 19860207
PRAI US 1985-699860       19850208; US 1986-898440       19860820
REP  EP 140521; US 4324683; US 4342826; US 4394449; US 4448882; US 4483921; US
     4483929
IC   C12N009-96; C12N011-02; C12Q001-54; G01N033-53
AB   WO    8604682 A UPAB: 19930922
     Assay reagent for determining an analyte (I) in a lipid vesicle
     immunoassay comprises a suspension of oligolamellar lipid vesicles containing
     encapsulated glucose 6-phosphate dehydrogenase (GPDH) at a specific
     activity of 1-15 units/ micromole vesicle lipid, and glucose 6-phosphate
     (II) at 2-50 mM.
          Each vesicle carries a surface array of ligand molecules to bind
     specifically and with high affinity to soluble antiligand molecules, to
     produce cell lyse and enzyme release from the liposomes in a reaction
     mixture containing serum complement.
          Homogeneous enzyme immunoassay system for determining. (I) in serum
     comprises an anti-(I) antibody; an assay reagent as defined above;
     complement to react with the vesicles, which have anti-(I) antibody bound
     to their surface; and a reporter system to react with released GPDH to
     give a spectral change.
          USE/ADVANTAGE - The enzyme is encapsulated at high specific activity
     and it is stable on storage of the reagent before use. Serum analytes such
     as theophylline, phenytoin, phenobarbital, digoxin and peptides can be
     determined conveniently with the system.
     0/6
FS   CPI EPI
FA   AB
MC   CPI: B01-D02; B03-H; B04-A06; B04-B01B; B04-B02C2; B04-B04D2;
          B04-B04D4; B05-A04; B05-B01M; B05-B01P; B11-C07A6;
          B11-C07B2; B12-K04A; B12-M11F; D05-A02A; D05-H09
     EPI: S03-E14H4

L123 ANSWER 6 OF 8  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   1986-112662 [17]   WPIX
DNN  N1986-083105       DNC C1986-048257
TI   Immunoassay using perturbed angular correlation spectroscopy - with
     complement mediated lysis of vesicles loaded with gamma-emitting cation.
DC   B04 D16 K08 P34 S03
IN   BALDESCHWI, J D; GAMBLE, R C; LIN, A M; TIN, G W
PA   (CALY) CALIFORNIA INST OF TECHN
CYC  1
PI   US 4581222      A  19860408 (198617)*        8              <--
PRAI US 1983-465360       19830209
IC   A61K043-00; A61R049-00; G01N033-54; G01T001-00
AB   US    4581222 A UPAB: 19930922
     A method for determining the concentration of an antigen in a sample comprises
     mixing together (a) the sample, (b) antibody to the antigen, (c) vesicles
     loaded with a gamma-emitting cation, and including on their surface an
     entity competitive with the antigen for the antibody and (c) complement
     and measuring the time integrated perturbation factor associated with the
     gamma-emitting cation. Also claimed is a method for determining the
     immunological response in vivo in a subject vertebrate by (a) injecting
     the vertebrate with antigen sensitised vesicles loaded a gamma-emitting
     cation and (b) measuring the time integrated perturbation factor for the
     gamma-emitting cation.
          USE/ADVANTAGE - The method is sensitive, specific and does not
     require separation of bound and unbound antigen. It can be applied in vivo and
     is relatively non-invasive in that it requires the injection of only small
     amts. of label and does not require the withdrawal of appreciable samples
     of the subject's own fluids.
     0/4
FS   CPI EPI GMPI
FA   AB
MC   CPI: B04-B01B; B04-B04C; B05-A04; B05-B01P; B11-C07A3;
          B11-C07A6; B12-K04; B12-M11D; D05-H09; K09-B; K09-E
     EPI: S03-E14H4

L123 ANSWER 7 OF 8  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   1985-012102 [02]   WPIX
DNN  N1985-008730        DNC C1985-005133
TI   Visualisation of target molecules in biological materials - by combination
     with visualisation polymer with active site(s).
DC   A96 B04 J04 S03
IN   BRIGATI, J D; LEARY, J J; WARD, C D; BRIGATI, D J; WARD, D C; LEARYJJ
PA   (UYYA) UNIV YALE
CYC  18
PI   WO 8404970      A  19841220 (198502)* EN   93
        RW: AT BE CH DE FR GB LU NL SE
         W: AU DK JP NO
     AU 8431503      A  19850104 (198513)
     EP 149654       A  19850731 (198531)  EN
         R: AT BE CH DE
     JP 60501573     W  19850919 (198544)
     DK 8500599      A  19850208 (198621)
     ES 8606656      A  19861001 (198649)
     US 4687732      A  19870818 (198735)                       <--
     CA 1237369      A  19880531 (198826)
     IL 72096        A  19891215 (199009)
     EP 149654       B1 19920909 (199237)  EN   56    G01N033-50     <--
         R: AT BE CH DE FR GB LI LU NL SE
     DE 3485918      G  19921015 (199243)             G01N033-50     <--
     DK 167162       B  19930906 (199341)             G01N033-545    <--
ADT  WO 8404970 A WO 1984-US888 19840608; EP 149654 A EP 1984-902738 19840608;
     JP 60501573 W JP 1984-502693 19840608; ES 8606656 A ES 1984-533313
     19840611; US 4687732 A US 1983-503298 19830610; EP 149654 B1 EP
     1984-902738 19840608, WO 1984-US888 19840608; DE 3485918 G DE 1984-3485918
     19840608, EP 1984-902738 19840608, WO 1984-US888 19840608; DK 167162 B WO
     1984-US888 19840608, DK 1985-599 19850208
FDT  EP 149654 B1 Based on WO 8404970; DE 3485918 G Based on EP 149654, Based
     on WO 8404970; DK 167162 B Previous Publ. DK 8500599
PRAI US 1983-503298        19830610
REP  EP 77671; FR 2295426; SSR880629; US 3690834; US 3853987; US 3996345; US
     4174384; US 4220450; US 4228237; US 4289747; US 4358535; US 4373932; US
     4434150
IC   ICM  G01N033-50; G01N033-545
     ICS  G01N033-52; G01N033-536; G01N033-58
AB   WO     8404970 A UPAB: 19930925
     Method for visualisation of the presence of an (in)organic target molecule
     in a biological material, comprises combination of the target with a
     visualisation polymer comprising multiple units of a monomer directly
     bonded together or linked by a coupling agent through chemical gps. or
     backbone moieties of the units.
          The visualisation monomer has at least 1 visualisation site and is an
     enzyme, a tagged, natural or synthetic polypeptide, a tagged polyol,
     polyolefin or carbohydrate. The chemical gp. is NH2, oxidised, 1,2-diol,
     COOH, SH, OH or a C-H bond. The back bone moiety is an amide bond, a C-C
     bond, C-O bond or C-H bond. The chemical gp. or backbone moiety is in the
     monomer at a position at least 1 atom away from the visualisation site of
     the monomers.
          USE/ADVANTAGE - The method is valuable for medical diagnosis, especially
     when it involves detection of very small amounts of material in biological
     materials. The visualisation polymers amplify the target molecules, and
     tags may be present to assist the visualisation.
     0/0
FS   CPI EPI
FA   AB
MC   CPI: A12-V03C; A12-W11; B02-Z; B04-B01B; B04-B02C; B04-B02D;
          B04-B03; B04-B04A; B04-B04C; B04-C01; B04-C02; B04-C03B; B04-D01;
          B11-C07; B11-C07B; B12-K04; J04-B01B
     EPI: S03-E14H4

L123 ANSWER 8 OF 8  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   1982-18203E [10]   WPIX
TI   Binding assays for tumour-associated glyco cpds. - using lectin as binding
     reagent.
DC   A96 B04 J04 S03
IN   ADACHI, M
PA   (NIKO-N) NIPPON KOTAI KENKYU; (SAKA) OTSUKA PHARM CO LTD
CYC  10
PI   FR 2487984      A  19820205 (198210)*      35
     NL 8103606      A  19820216 (198211)
     GB 2083623      A  19820324 (198212)
     DK 8103393      A  19820308 (198213)
     JP 57029949     A  19820218 (198213)
     DE 3129923      A  19820408 (198215)
     SE 8104597      A  19820607 (198225)
     DE 3129923      C  19840620 (198426)
     GB 2083623      B  19840926 (198439)
     US 4571382      A  19860218 (198610)                       <--
     JP 61016945     B  19860502 (198622)
     CH 658132       A  19861015 (198646)
     SE 453947       B  19880314 (198813)
     IT 1143216      B  19861022 (198830)
ADT  GB 2083623 A GB 1981-23381 19810730; JP 57029949 A JP 1980-104786
     19800730; DE 3129923 A DE 1981-3129923 19810729; US 4571382 A US
     1981-288445 19810730
PRAI JP 1980-104786          19800730
IC   C12Q001-00; G01N033-58
AB   FR   2487984 A UPAB: 19930915
     Processes are claimed for determn. of tumour-associated glyco cpds. (TAG),
     i.e. glycoproteins, glycopeptides, glycolipids and/or sugars with terminal
     galactose-(beta-1 to 3 or beta-1 to 4)-N-acetylglucosamine or -N-acetyl
     galactosamine gps., in physiological fluids.
          Process (A) comprises (a) contacting the test sample with a known
     amount of immobilised TAG (or analogue) and a known amount of a labelled
     lectin; (b) separating the phases; and (c) measuring the activity of the
     label in one of the phases. Process (B) comprises (a) contacting the test
     sample with a known amount of labelled TAG (or analogue) and a known amount of
     opt. immobilised lectin; (b) separating TAG-lectin complex from unbound
     TAG; and (c) measuring the activity of the label in one of the fractions.
     Process (C) comprises (a) contacting the test sample with immobilised
     lectin to form an immobilised lectin-TAG complex; (b) reacting the complex
     with a known amount of labelled lectin; (c) separating the phases; and (d)
     measuring the activity of the label in one of the phases (N.B. As claimed,
     the last step in the processes comprises measuring the activity of the
     label in each of the phases or fractions).
          The processes can be used for cancer diagnosis, since cancer is
     associated with higher TAG levels than normal.
FS   CPI EPI
FA   AB
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MC    CPI: A12-V03C; B04-B01B; B04-B02C; B04-B04A; B04-C01; B04-C02;
           B05-A04; B11-C07; B12-K04; J04-B01
      EPI: S03-E14H1

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=> d all l132 tot

L132 ANSWER 1 OF 7  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2005-090412 [10]   WPIX
CR   2002-055599 [07]
DNC  C2005-030484
TI   Modulating growth of a cell, useful for treatment and prophylaxis of
     cancer, comprises contacting the cell with an agent to modulate functional
     activity of sphingosine kinase.
DC   B04 B05 D16
IN   GAMBLE, J; SUKOCHEVA, O; VADAS, M; WANG, L; XIA,
     P
PA   (MEDV-N) MEDVET SCI PTY LTD
CYC  1
PI   US 2005009732   A1 20050113 (200510)*      35    A61K038-17
ADT  US 2005009732 A1 Provisional US 2003-447707P 20030219, CIP of US
     2003-275686 20030625, US 2004-780897 20040219
PRAI AU 2003-900729       20030219
IC   ICM  A61K038-17
AB   US2005009732 A UPAB: 20050211
     NOVELTY - Modulating the growth of a cell comprises contacting the cell
     with an agent for a time and under conditions sufficient to modulate the
     functional activity of sphingosine kinase.
          DETAILED DESCRIPTION - Modulating the growth of a cell comprises
     contacting the cell with an agent for a time and under conditions
     sufficient to modulate the functional activity of sphingosine
     kinase, where down-regulation of the functional activity of
     sphingosine kinase down-regulates the growth and up-regulation of
     the functional activity of the sphingosine kinase up-regulates
     the cell growth. The down-regulation is to an oncogenic ineffective level,
     while the up-regulation is to an oncogenic effective level.
          INDEPENDENT CLAIMS are included for the following:
          (1) method for treatment or prophylaxis of a condition characterized
     by aberrant, unwanted or otherwise inappropriate cell growth in a mammal
     by administering the agent as above;
          (2) a composition comprising the agent together with a carrier and/or
     diluents; and
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          (3) a method of diagnosing a condition or a predisposition or
     resistance to a condition characterized by aberrant, unwanted or otherwise
     inappropriate cell growth in a mammal comprising screening a biological
     sample from the mammal for the presence of sphingosine kinase or
     a nucleic acid molecule encoding sphingosine kinase.
          ACTIVITY - Cytostatic.
          No biological data given.
          MECHANISM OF ACTION - Sphingosine kinase modulator.
          USE - The methods, compositions and kinases are useful for the
     treatment or prophylaxis of a condition characterized by aberrant,
     unwanted or otherwise inappropriate cell growth in a mammal (claimed),
     e.g. cancer of the colon, stomach, lung, brain, bone, esophagus, pancreas,
     breast, ovary or uterus.
          ADVANTAGE - Modulation of sphingosine kinase allows a novel
     approach to treatment of cellular proliferation.
     Dwg.0/11
FS   CPI
FA   AB; DCN
MC   CPI: B04-B04D; B04-B04L; B04-E03E; B04-L04C; B10-B03B; B11-C08E3;
          B11-C08E5; B12-K04A1; B14-H01B; B14-L01; B14-L06; D05-H08; D05-H09

L132 ANSWER 2 OF 7  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2003-646055 [61]   WPIX
DNC  C2003-176771
TI   Pharmaceutical composition useful for treating immune mediated disease,
     e.g. bone marrow, comprising sphingosine 1-phosphate/endothelial
     differentiation gene receptor agonist.
DC   B05
IN   DOHERTY, G A; FORREST, M J; HAJDU, R; HALE, J J; LI, Z; MANDALA, S M;
     MILLS, S G; ROSEN, H; SCOLNICK, E M; ZHEN, L
PA   (MERI) MERCK & CO INC; (DOHE-I) DOHERTY G A; (FORR-I) FORREST M J;
     (HAJD-I) HAJDU R; (HALE-I) HALE J J; (MAND-I) MANDALA S M;
     (MILL-I) MILLS S G; (ROSE-I) ROSEN H; (ZHEN-I) ZHEN L; (SCOL-I) SCOLNICK E
     M
CYC  102
PI   WO 2003061567    A2 20030731 (200361)* EN  101    A61K000-00
        RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS
            LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KR KZ
            LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO
            RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM
            ZW
     AU 2003216054    A1 20030902 (200422)              A61K000-00
     US 2004058894    A1 20040325 (200422)              A61K031-66
     EP 1469863       A2 20041027 (200471)  EN          A61K031-662
         R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LI LT LU LV
            MC MK NL PT RO SE SI SK TR
     US 2005070506    A1 20050331 (200524)              A61K031-66
ADT  WO 2003061567 A2 WO 2003-US1120 20030114; AU 2003216054 A1 AU 2003-216054
     20030114; US 2004058894 A1 Provisional US 2002-349991P 20020118, US
     2003-339380 20030109; EP 1469863 A2 EP 2003-731917 20030114, WO
     2003-US1120 20030114; US 2005070506 A1 Provisional US 2002-349991P
     20020118, Provisional US 2002-362566P 20020307, Provisional US
     2002-382933P 20020523, WO 2003-US1120 20030114, US 2004-501176 20040712
FDT  AU 2003216054 A1 Based on WO 2003061567; EP 1469863 A2 Based on WO
     2003061567
PRAI US 2002-382933P      20020523; US 2002-349991P      20020118;
     US 2002-362566P      20020307; US 2003-339380       20030109;
     US 2004-501176       20040712
IC   ICM  A61K000-00; A61K031-66; A61K031-662
AB   WO2003061567 A UPAB: 20030923
     NOVELTY - A pharmaceutical composition comprises sphingosine
     1-phosphate (S1P1)/endothelial differentiation genes (Edg1) receptor
     agonist (I) and a carrier. The agonist has a selectivity for the S1P1/Edg1
     receptor over the S1PR3/Edg3 receptor of at least 100 fold, and has an
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EC50 for binding S1P1/Edg1 receptor of at most 10 nM (as evaluated in the 35-GTP gamma -S binding assay).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) pharmaceutical composition comprising compound having S1P1/Edg1 receptor agonist activity (excluding a compound of formula (II), its salt or hydrate) and a carrier. The compound has a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor at least 20 fold, and has an EC50 for binding S1P1/Edg1 receptor of at most 100 nM (as evaluated in the 35-GTP gamma -S binding assay);

(2) identification (M1) of (I) comprising:

(a) providing first receptor preparation comprising recombinant cell (c1) expressing the S1P1/Edg1 receptor or functional equivalent of the S1P1/Edg1 receptor capable of binding to S1P; or a membrane preparation of (c1);

(b) providing second receptor preparation comprising recombinant cell (c2) expressing the S1P3/Edg3 receptor or functional equivalent of the S1P3/Edg3 receptor capable of binding to S1P; or a membrane preparation of (c2);

(c) separately contacting the cells or membrane preparations with the candidate compound; and

(d) determining whether the compound binds to and activates the S1P1/Edg1 and S1P3/Edg3 receptors by measuring the level of a signal generated from the interaction of the compound with each receptor; and

(3) treatment (M2) of respiratory diseases comprising administering (I).

X = O, S, NR1, or (CH2)1-2 (optionally mono- to tetra- substituted by halo);

R1, R2 = H, 1-4C alkyl or halo(1-4C)alkyl;

R1a = 1-4C alkyl or O(1-4C)alkyl (both optionally mono- to tri-substituted by halo), H or OH;

R1b = H, OH, 1-4C alkyl or halo(1-4C)alkyl;

R3 = H, OH, halo, 1-4C alkyl, O-1-4C alkyl, O-halo-1-4C alkyl, or hydroxy(1-4C)alkyl;

Y' = -CH2-, -C(O)-, -CH(OH)-, -C(=NOH)-, O or S; and

R4 = 4-14C alkyl or 4-14C alkenyl.

ACTIVITY - Dermatological; Antiinflammatory; Immunosuppressive; Antirheumatic; Antiarthritic; Antidiabetic; Hepatotropic; Ophthalmological; Neuroprotective; Antiulcer; Antipsoriatic; Antiasthmatic; Thyromimetic; Antipyretic; Antiseborrheic; Antipruritic; Vasotropic; Antiallergic; Thrombolytic; Antimigraine; Nephrotropic; Cytostatic; Antianemic; Hemostatic; Osteopathic; Antiarteriosclerotic; Antialopecia; Antibacterial; Virucide; Anti-HIV; Tranquilizer; Antitussive; Vulnerary.

MECHANISM OF ACTION - **Sphingosine** 1-phosphate (S1P1)/endothelial differentiation genes (Edg1) receptor agonist; Lymphocyte infiltration inhibitor; Airway function modulator.

The activity of (3-(4-octyloxy-benzylamino)-propyl)-phosphonic acid (A) in GTP gamma -S binding was assessed using human S1P1/Edg1 receptor. (A) showed an EC50 value of 1.5 nM.

USE - For treating immunoregulatory abnormality (e.g. systemic lupus erythematosus, chronic rheumatoid arthritis, type I diabetes mellitus, inflammatory bowel disease, biliary cirrhosis, uveitis, multiple sclerosis, Crohn's disease, ulcerative colitis, bullous pemphigoid, sarcoidosis, psoriasis, autoimmune myositis, Wegener's granulomatosis, ichthyosis, Graves ophthalmopathy, bone marrow or organ transplant rejection or graft-versus-host disease, Hashimoto's thyroiditis, myasthenia gravis, allergic encephalomyelitis, glomerulonephritis, rheumatic fever, inflammatory and hyperproliferative skin diseases, dermatitis, lichen planus, pemphigus, epidermolysis bullosa, urticaria, angioedemas, vasculitis, erythema, cutaneous eosinophilia, acne, keratoconjunctivitis, vernal conjunctivitis, uveitis associated with Behcet's disease, keratitis, conical cornea, dystrophia epithelialis corneae, corneal leukoma, ocular pemphigus, Mooren's ulcer, scleritis, Vogt-Koyanagi-Harada syndrome, pollen allergies, asthma, airway hyper-responsiveness, gastric ulcers, vascular damage, ischemic bowel diseases, necrotizing enterocolitis, intestinal lesions associated with thermal burns, coeliac diseases, proctitis, eosinophilic gastroenteritis, mastocytosis, migraine, rhinitis, eczema, interstitial nephritis, Goodpasture's syndrome, hemolytic-uremic syndrome, diabetic nephropathy, multiple myositis, Guillain-Barre syndrome, Meniere's disease, mono-, poly- and multiple-polyneuritis, radiculopathy, hyperthyroidism, Basedow's disease, pure red cell aplasia, aplastic anemia, hypoplastic anemia, idiopathic thrombocytopenic purpura, agranulocytosis, anerythroplasia, osteoporosis, fibroid lung, idiopathic interstitial pneumonia, dermatomyositis, leukoderma vulgaris, photoallergic sensitivity, cutaneous T cell lymphoma, arteriosclerosis, atherosclerosis, aortitis syndrome, polyarteritis nodosa, myocardosis, scleroderma, Wegener's granuloma, Sjogren's syndrome, adiposis, eosinophilic fascitis, lesions of gingiva, periodontium, alveolar bone, substantia ossea dentis, glomerulonephritis, male pattern alopecia or alopecia senilis, muscular dystrophy, pyoderma and Sezary's syndrome, Addison's disease, ischemia-reperfusion injury of organs, transplantation or ischemic disease, endotoxin-shock, pseudomembranous colitis, ischemic acute renal insufficiency, chronic renal insufficiency, toxinosis caused by lung-oxygen or drugs, lung cancer, pulmonary emphysema, cataracta, siderosis, retinitis pigmentosa, senile macular degeneration, vitreal scarring, corneal alkali burn, dermatitis erythema multiforme, linear IgA ballous dermatitis and cement dermatitis, gingivitis, periodontitis, sepsis, pancreatitis, diseases caused by environmental pollution, aging, carcinogenesis, metastasis of carcinoma and hypobaropathy, disease caused by histamine or leukotriene-C4 release, autoimmune hepatitis, primary biliary cirrhosis, sclerosing cholangitis, partial liver resection, necrosis, viral hepatitis, shock, or anoxia, alcoholic cirrhosis, hepatic failure, augmentation of chemotherapeutic effect, cytomegalovirus infection, HCMV infection, AIDS, cancer, senile dementia, trauma, and chronic bacterial infection); and for treating respiratory diseases or conditions (e.g. chronic obstructive pulmonary disease, adult/infant respiratory distress syndrome, cough, eosinophilic granuloma, respiratory syncytial virus bronchiolitis, idiopathic pulmonary fibrosis and acute lung injury) (all claimed).

ADVANTAGE - (I) Has a selectivity for the S1P1/Edg1 receptor over the S1PR3/Edg3 receptor at least 100 (preferably 200, especially 500, particularly 2000) fold as measured by the ratio of EC50 for the S1P1/Edg1 receptor to the EC50 for the S1P3/Edg3 receptor in the 35-GTP gamma -S binding assay. The compound possesses an EC50 for binding S1P1/Edg1 receptor of at most 1 nM (as evaluated in the 35-GTP gamma -S binding assay).

Dwg.0/0

FS CPI

FA AB; GI; DCN

MC CPI: **B04-B01B**; B04-F0100E; B04-M01; B05-B01E; B05-B01F; B07-H; B11-C07; B11-C08; B12-K04; B14-A01; B14-A02; B14-C01; B14-C03; B14-C04; B14-C06; B14-C09B; B14-D01; B14-E08; B14-E10; B14-F02; B14-F03; B14-F05; B14-F07; B14-F08; B14-G01; B14-G02; B14-H01; B14-J01; B14-J01A4; B14-J01B4; B14-J05C; B14-K01; B14-L01; B14-L04; B14-L05; B14-L06; B14-L08; B14-L09; B14-M01; B14-N01; B14-N02; B14-N03; B14-N04; B14-N06; B14-N10; B14-N11; B14-N12; B14-N13; B14-N16; B14-N17; B14-R02; B14-S01; B14-S04; B14-S06

L132 ANSWER 3 OF 7 WPIX COPYRIGHT 2005 THE THOMSON CORP on STN

AN 2003-201282 [19] WPIX

DNC C2003-051124

TI Modulating cytokine- or tumor necrosis factor-induced cellular activity, useful for treating or preventing a neoplastic condition, comprises modulating an intracellular **sphingosine** kinase-dependent signaling mechanism.

DC B04 D16

IN **GAMBLE, J**; MORETTI, P; **PITSON, S**; **VADAS, M**; WANG, L; **XIA, P**

PA (MEDV-N) MEDVET SCI PTY LTD; (XIAP-I) XIA P

CYC 101

PI WO 2002098458 A1 20021212 (200319)* EN 96 A61K039-395

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        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZM ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT
            RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZM
            ZW
     EP 1404364       A1 20040407 (200425)  EN        A61K039-395
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     AU 2002304973    A1 20021216 (200452)            A61K039-395
     JP 2005502598    W  20050127 (200510)     135    A61K045-00
     US 2005100547    A1 20050512 (200532)            A61K039-395
ADT  WO 2002098458 A1 WO 2002-AU710 20020603; EP 1404364 A1 EP 2002-732213
     20020603, WO 2002-AU710 20020603; AU 2002304973 A1 AU 2002-304973
     20020603; JP 2005502598 W WO 2002-AU710 20020603, JP 2003-501495 20020603;
     US 2005100547 A1 WO 2002-AU710 20020603, US 2004-479933 20041014
FDT  EP 1404364 A1 Based on WO 2002098458; AU 2002304973 A1 Based on WO
     2002098458; JP 2005502598 W Based on WO 2002098458
PRAI AU 2001-9759          20011227; AU 2001-5521          20010607;
     AU 2001-6978          20010813
IC   ICM  A61K039-395; A61K045-00
     ICS  A61K038-19; A61K038-45; A61P029-00; A61P035-00; A61P043-00;
          C12N005-06; C12Q001-02; C12Q001-48; G01N033-15; G01N033-50
AB   WO 200298458 A UPAB: 20030320
     NOVELTY - Modulating cytokine-induced or tumor necrosis factor
     (TNF)-induced cellular activity, comprises contacting the cell with an
     agent under conditions sufficient to modulate the interaction of
     sphingosine kinase with a TNF receptor-associated factor (TRAF),
     preferably TRAF2, where inducing the association up-regulates cellular
     activity, and inhibiting the association down-regulates cellular activity.
          DETAILED DESCRIPTION - Modulating cytokine-induced or tumor necrosis
     factor (TNF)-induced cellular activity, comprises contacting the cell with
     an agent for a time and under conditions sufficient to modulate the
     interaction of sphingosine kinase with a TNF receptor-associated
     factor (TRAF), preferably TRAF2, where inducing or agonizing the
     association up-regulates the cellular activity, and inhibiting or
     antagonizing the association down-regulates the cellular activity.
          INDEPENDENT CLAIMS are included for the following:
          (1) treating and/or preventing a condition of aberrant, unwanted or
     inappropriate cytokine-induced or tumor necrosis factor (TNF)-induced
     cellular activity in a mammal;
          (2) detecting an agent capable of modulating the interaction of TRAF
     with sphingosine kinase or its functional equivalent or
     derivative;
          (3) analyzing, designing and/or modifying an agent capable of
     interacting with the TRAF binding site of sphingosine kinase or
     its derivative and modulating at least one functional activity associated
     with the sphingosine kinase;
          (4) an agent described or identified in the methods cited above; and
          (5) a pharmaceutical condition comprising the modulatory agent
     described in the methods above, and one or more pharmaceutical carriers
     and/or diluents;
          ACTIVITY - Cytostatic; Antiinflammatory; Antirheumatic;
     Antiarthritic.
          No biological data given.
          MECHANISM OF ACTION - Sphingosine Kinase Inhibitor;
     Sphingosine Kinase Stimulator; TRAF Agonist 2; TRAF Antagonist 2.
          USE - The agent is useful for manufacturing a medicament for treating
     a mammal with a condition of aberrant, unwanted or inappropriate
     cytokine-induced or tumor necrosis factor (TNF)-induced cellular activity
     (claimed). The methods are useful for modulating cytokine-induced or
     TNF-induced cellular activity, or for treating or preventing a condition
     of aberrant, unwanted or inappropriate cytokine-induced or TNF-induced
     cellular activity in a mammal, such as neoplastic condition or
     inflammation (e.g. rheumatoid arthritis).
     Dwg.0/9
FS   CPI
FA   AB; DCN
MC   CPI: B04-C01A; B04-L04; B11-C08; B11-C10; B14-C03; B14-C09B; B14-D06;
          B14-H01; B14-L01; B14-L06; D05-A02B; D05-H09

L132 ANSWER 4 OF 7  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2002-362301 [39]   WPIX
DNC  C2002-102538
TI   Cancer screening, involves detecting sphingosine-1-phosphate, by
     reacting a sample with an enzyme to cleave it into a long chain aldehyde
     and ethanolamine-1-phosphate.
DC   B04 D16
IN   JOHNSON, J L; PARROTT, J A; SKINNER, M K
PA   (ATAI-N) ATAIRGIN TECHNOLOGIES INC; (JOHN-I) JOHNSON J L;
     (PARR-I) PARROTT J A; (SKIN-I) SKINNER M K; (LPLT-N) LPL TECHNOLOGIES INC
CYC  97
PI   WO 2002022078   A2 20020321 (200239)* EN   22    A61K000-00
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO
            RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG UZ VN YU ZA ZW
     AU 2001090946   A  20020326 (200251)             A61K000-00
     US 2002127628   A1 20020912 (200262)             C12Q001-66
     US 6448023      B1 20020910 (200263)             C12Q001-66
     US 6716595      B2 20040406 (200425)             C12Q001-66
ADT  WO 2002022078 A2 WO 2001-US28807 20010913; AU 2001090946 A AU 2001-90946
     20010913; US 2002127628 A1 Div ex US 2000-661988 20000914, US 2002-133012
     20020426; US 6448023 B1 US 2000-661988 20000914; US 6716595 B2 Div ex US
     2000-661988 20000914, US 2002-133012 20020426
FDT  AU 2001090946 A Based on WO 2002022078; US 6716595 B2 Div ex US 6448023
PRAI US 2000-661988        20000914; US 2002-133012        20020426
IC   ICM  A61K000-00; C12Q001-66
     ICS  C12Q001-00; C12Q001-26; C12Q001-42; G01N033-53
AB   WO 200222078 A UPAB: 20020621
     NOVELTY - Cancer screening, comprising detecting sphingosine 1
     phosphate (S1P) involves reacting a sample with an enzyme to cleave S1P to
     a mixture of ethanolamine-1-phosphate and long-chain aldehyde, subjecting
     the mixture to a second enzymatic reaction to produce a detectable signal
     and determining the concentration of S1P by measuring the signal, is new.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the
     following:
          (1) diagnosing carcinoma comprising assaying for the presence of S1P
     in a sample; and
          (2) a diagnostic kit for detecting the concentration of S1P.
          USE - For screening for breast, ovarian, cervical, uterine,
     endometrial, peritoneal and fallopian tube carcinoma.
     Dwg.0/0
FS   CPI
FA   AB; DCN
MC   CPI: B01-B03; B04-B01B; B04-L03C; B04-L06; B05-B01P; B07-A02B;
          B07-A03; B11-C08; B12-K04A1; D05-A02D; D05-H09

L132 ANSWER 5 OF 7  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2002-130896 [17]   WPIX
DNC  C2002-040274
TI   Novel sphingosine kinase variants which exhibit reduced
     catalytic activity useful for modulating cellular functional activity and
     treating or preventing inflammatory, degenerative diseases and neoplastic
     conditions.
DC   B04 D16
IN   MORETTI, P; PITSON, S; VADAS, M; WATTENBERG, B
     ; XIA, P; D'ANDREA, R; GAMBLE, J; ZEBOL, J; DANDREA, R
PA   (MEDV-N) MEDVET SCI PTY LTD
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CYC  97
PI   WO 2002000887    A1 20020103 (200217)* EN  104    C12N015-54
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
            SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
     AU 2001065699    A   20020108 (200235)              C12N015-54
     NO 2002006265    A   20030224 (200321)              C12N000-00
     EP 1299548       A1  20030409 (200325)  EN          C12N015-54
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     CN 1444654       A   20030924 (200382)              C12N015-54
     JP 2004500903    W   20040115 (200410)       150    C12N015-09
     ZA 2003000214    A   20040630 (200448)       118    C12N000-00
     BR 2001012059    A   20040727 (200452)              C12N015-54
     NZ 523343        A   20050324 (200523)              C12N015-54
ADT  WO 2002000887 A1 WO 2001-AU730 20010620; AU 2001065699 A AU 2001-65699
     20010620; NO 2002006265 A WO 2001-AU730 20010620, NO 2002-6265 20021227;
     EP 1299548 A1 EP 2001-942904 20010620, WO 2001-AU730 20010620; CN 1444654
     A CN 2001-813405 20010620; JP 2004500903 W WO 2001-AU730 20010620, JP
     2002-506202 20010620; ZA 2003000214 A ZA 2003-214 20030108; BR 2001012059
     A BR 2001-12059 20010620, WO 2001-AU730 20010620; NZ 523343 A NZ
     2001-523343 20010620, WO 2001-AU730 20010620
FDT  AU 2001065699 A Based on WO 2002000887; EP 1299548 A1 Based on WO
     2002000887; JP 2004500903 W Based on WO 2002000887; BR 2001012059 A Based
     on WO 2002000887; NZ 523343 A Div in NZ 535290, Based on WO 2002000887
PRAI AU 2001-2749          20010129; AU 2000-8408          20000628;
     AU 2000-8699          20000711; AU 2000-9980          20000908
IC   ICM  C12N000-00; C12N015-09; C12N015-54
     ICS  A61K038-43; A61K038-45; A61P001-04; A61P007-00; A61P009-10;
          A61P011-06; A61P019-02; A61P025-00; A61P029-00; A61P035-00;
          A61P043-00; C12N009-10; C12N009-12; C12Q001-02; C12Q001-48
AB   WO 200200887 A UPAB: 20020313
     NOVELTY - A sphingosine kinase variant (I), comprising a
     mutation in a sphingosine kinase binding region defined by amino
     acids 16-153 or a ATP binding site region (or their functionally
     equivalent regions), where the variant exhibits ablated or reduced
     catalytic activity relative to wild-type SK, or a derivative, homolog,
     analog, chemical equivalent or mimetic of the SK variant, is new.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
     following:
          (1) an isolated nucleic acid molecule (II), its derivative or
     equivalent, comprising a nucleotide sequence encoding or complementary to
     a sequence encoding (I);
          (2) detecting an agent capable of modulating the interaction of FOSK
     (friends of SK) with SK or its functional equivalent or derivative, by
     contacting a cell or its extract containing the SK or FOSK or its
     functional equivalent or derivative with a putative agent and detecting an
     altered expression phenotype associated with the interaction;
          (3) detecting an agent capable of binding or otherwise associating
     with the SK region defined by amino acid 16-153 (or its functional
     equivalent or derivative), by contacting a cell containing the amino acid
     region with a putative agent and detecting an altered expression phenotype
     associated with modulation of the function of SK;
          (4) analyzing, designing and/or modifying an agent capable of
     interacting with SK region defined by amino acid 16-153 or its derivative
     and modulating a functional activity associated with SK, by contacting SK
     or its derivative with a putative agent and assessing the degree of
     interactive complementarity of the agent with the binding site;
          (5) an agent (II) identified by the method of (2), (3) or (4); and
          (6) a pharmaceutical composition comprising (I) or (II).
          ACTIVITY - Antiinflammatory; Antirheumatic; Antiarthritic;
     Cytostatic; Antiasthmatic; Antiatherosclerotic; Neuroprotective;
     Antibacterial; Immunosuppressive; Osteopathic.
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          No biological data is given.
          MECHANISM OF ACTION - Modulator of SK/FOSK interactivity; Inhibitor
     of wild-type SK activation; Regulator of cellular functional activity
     including chemokine, cytokine and inflammatory modulator production; gene
     therapy.
          USE - (I) and (II) are useful for modulating cellular functional
     activity, down-regulating wild-type SK baseline activity and/or preventing
     wild-type SK activation. (I) and (II) are also useful for treatment and/or
     prophylaxis of a condition in a mammal, characterized by aberrant,
     unwanted or inappropriate cellular activity, and in the manufacture of a
     medicament for modulating cellular functional activity. (All claimed). (I)
     is useful in therapeutically or prophylactically treating inflammatory
     diseases (e.g. rheumatoid arthritis, inflammatory bowel disease),
     neoplastic conditions (e.g. solid cancer), asthma, atherosclerosis,
     meningitis, multiple sclerosis, septic shock, osteoarthritis, and other
     degenerative diseases.
     Dwg.0/15
FS   CPI
FA   AB; DCN
MC   CPI: B04-E02E; B04-F01; B04-L04; B11-C08E1; B11-C08E3; B12-K04E; B14-C06;
          B14-C09A; B14-C09B; B14-E10C; B14-F07; B14-H01; B14-H01B; B14-K01A;
          B14-N01; B14-N16; B14-S01; B14-S03A; B14-S05; D05-A02B; D05-H08;
          D05-H09; D05-H12B1

L132 ANSWER 6 OF 7  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN   2002-055599 [07]   WPIX
CR   2005-090412 [10]
DNC  C2002-015960
TI   Modulating cell growth, especially for treating colon, stomach, lung,
     brain, bone, esophagus, pancreas, breast, ovary or uterine cancer,
     comprises administration of a sphingosine kinase modulator.
DC   B04 D16
IN   GAMBLE, J; VADAS, M; WANG, L; XIA, P
PA   (MEDV-N) MEDVET SCI PTY LTD; (GAMB-I) GAMBLE J; (VADA-I) VADAS M; (WANG-I)
     WANG L; (XIAP-I) XIA P
CYC  97
PI   WO 2001085953   A1 20011115 (200207)* EN   56    C12N015-54
        RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ
            NL OA PT SD SE SL SZ TR TZ UG ZW
         W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
            DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
            KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
            SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
     AU 2001056001   A  20011120 (200219)
     NO 2002005375   A  20030107 (200317)             C12N015-54
     EP 1290182      A1 20030312 (200320)  EN          C12N015-54
         R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
            RO SE SI TR
     BR 2001010759   A  20030506 (200334)             C12N015-54
     CN 1436241      A  20030813 (200373)             C12N015-54
     JP 2003532423   W  20031105 (200377)       52    C12N015-09
     US 2004014635   A1 20040122 (200407)             A61K031-00
     ZA 2002009066   A  20040630 (200448)       70    C12N000-00
ADT  WO 2001085953 A1 WO 2001-AU539 20010511; AU 2001056001 A AU 2001-56001
     20010511; NO 2002005375 A WO 2001-AU539 20010511, NO 2002-5375 20021108;
     EP 1290182 A1 EP 2001-929118 20010511, WO 2001-AU539 20010511; BR
     2001010759 A BR 2001-10759 20010511, WO 2001-AU539 20010511; CN 1436241 A
     CN 2001-810962 20010511; JP 2003532423 W JP 2001-582542 20010511, WO
     2001-AU539 20010511; US 2004014635 A1 WO 2001-AU539 20010511, US
     2003-275686 20030625; ZA 2002009066 A ZA 2002-9066 20021107
FDT  AU 2001056001 A Based on WO 2001085953; EP 1290182 A1 Based on WO
     2001085953; BR 2001010759 A Based on WO 2001085953; JP 2003532423 W Based
     on WO 2001085953
PRAI AU 2000-7447          20000511
IC   ICM  A61K031-00; C12N000-00; C12N015-09; C12N015-54
     ICS  A61K031-13; A61K031-133; A61K035-14; A61K038-00; A61K045-00;
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          A61P035-00; A61P043-00; C12N005-06; C12N005-10; C12Q001-02;
          C12Q001-48; C12Q001-68
AB     WO 200185953 A UPAB: 20050211
       NOVELTY - Modulating cell growth, comprising administering an agent to
       modulate the functional activity of sphingosine kinase, is new.
            DETAILED DESCRIPTION - INDEPENDENT CLAIMS are included for the
       following:
            (1) compositions for use in the novel method; and
            (2) diagnosing a condition or predisposition to a condition
       characterized by inappropriate cell growth comprising screening a sample
       for the presence of sphingosine kinase or a molecule encoding
       sphingosine kinase.
            ACTIVITY - Cytostatic.
            No biological data is given.
            MECHANISM OF ACTION - Sphingosine kinase modulation.
            USE - For controlling proliferation of cells, including uncontrolled
       proliferation of neoplastic/malignant cells (especially from the colon,
       stomach, lung, brain, bone, esophagus, pancreas, breast, ovary or uterus.
       The malignant cell may be transfected due to up-regulation of an oncogene,
       especially Ras. (All claimed).
       Dwg.0/4
FS     CPI
FA     AB; DCN
MC     CPI: B04-B01B; B04-L04; B05-B01P; B10-B03B; B11-C08E3;
            B12-K04A1; B14-H01; B14-H01B; B14-N01; B14-N13; B14-N16; D05-H09

L132 ANSWER 7 OF 7  WPIX  COPYRIGHT 2005 THE THOMSON CORP on STN
AN     2001-016227 [02]   WPIX
DNC    C2001-004532
TI     Novel sphingosine kinase protein and nucleic acid molecules for
       diagnosis, prophylaxis and treatment of rheumatoid arthritis, asthma,
       atherosclerosis, inflammation, meningitis, multiple sclerosis and septic
       shock.
DC     B04 D16
IN     D'ANDREA, R J; GAMBLE, J R; PITSON, S M; VADAS, M
       A; WATTENBERG, B W; XIA, P; DANDREA, R J
PA     (JOHJ) JOHNSON & JOHNSON RES PTY LTD; (JOHJ) JOHNSON &
       JOHNSON PHARM RES & DEV LLC; (JOHJ) JOHNSON & JOHNSON PHARM R &
       D LLC
CYC    93
PI     WO 2000070028    A1 20001123 (200102)* EN  100    C12N009-12
          RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL
              OA PT SD SE SL SZ TZ UG ZW
           W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ
              EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK
              LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI
              SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW
       AU 2000045239    A  20001205 (200113)
       EP 1192247       A1 20020403 (200230)  EN           C12N009-12
           R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
              RO SE SI
       KR 2002000805    A  20020105 (200244)               C12N009-12
       JP 2002543831    W  20021224 (200313)       101     C12N015-09
       US 6730480       B1 20040504 (200430)               C12Q001-68
       US 2004132053    A1 20040708 (200445)               C12Q001-68
       NZ 515132        A  20050128 (200513)               C12N009-12
       AU 780746        B2 20050414 (200530)               C12N009-12
ADT    WO 2000070028 A1 WO 2000-AU457 20000512; AU 2000045239 A AU 2000-45239
       20000512; EP 1192247 A1 EP 2000-926537 20000512, WO 2000-AU457 20000512;
       KR 2002000805 A WO 2000-AU457 20000512, KR 2001-714462 20011113; JP
       2002543831 W JP 2000-618434 20000512, WO 2000-AU457 20000512; US 6730480
       B1 WO 2000-AU457 20000512, US 2002-959897 20020124; US 2004132053 A1 Div
       ex WO 2000-AU457 20000512, Div ex US 2002-959897 20020124, US 2003-642289
       20030818; NZ 515132 A NZ 2000-515132 20000512, WO 2000-AU457 20000512; AU
       780746 B2 AU 2000-45239 20000512
FDT    AU 2000045239 A Based on WO 2000070028; EP 1192247 A1 Based on WO
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     2000070028; KR 2002000805 A Based on WO 2000070028; JP 2002543831 W Based
     on WO 2000070028; US 6730480 B1 Based on WO 2000070028; US 2004132053 A1
     Div ex US 6730480; NZ 515132 A Based on WO 2000070028; AU 780746 B2
     Previous Publ. AU 2000045239, Based on WO 2000070028
PRAI AU 1999-1504          19990708; AU 1999-339          19990513
IC   ICM  C12N009-12; C12N015-09; C12Q001-68
     ICS  A61K031-711; A61K038-43; A61K038-45; A61K038-55; A61K039-395;
          A61K045-00; A61K048-00; A61P009-10; A61P011-06; A61P025-00;
          A61P025-28; A61P029-00; A61P031-10; A61P043-00; C07H021-04;
          C07K016-18; C07K016-40; C12N001-20; C12N005-00; C12N005-10;
          C12N009-96; C12N015-00; C12P021-08; C12Q001-48; G01N033-53;
          G01N033-577
AB   WO 200070028 A UPAB: 20040621
     NOVELTY - An isolated sphingosine kinase (SK) protein (I) or its
     derivative, analog, chemical equivalent or mimetic, is new.
          DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
     following:
          (1) an isolated nucleic acid molecule (II) or its derivative or
     analog comprising a nucleotide sequence encoding or complementary to a
     sequence encoding (I);
          (2) an agent (III) for use in modulating SK activity or expression;
          (3) a pharmaceutical composition comprising (I) or (III);
          (4) an isolated antibody (IV) directed to (I) or (II); and
          (5) diagnosing or monitoring a mammalian disease condition by
     screening for (I) in a biological sample isolated from the mammal.
          ACTIVITY - Antiarthritic; Antiasthmatic; Antiarteriosclerotic;
     Antiinflammatory; Neuroprotective; Antibacterial; Immunosuppressive.
          No supporting data is given.
          MECHANISM OF ACTION - Modulator of sphingosine kinase
     activity or expression.
          USE - (I), (II) and (III) are useful for modulating expression,
     functional activity or cellular functional activity of sphingosine
     kinase in a subject and also for treating a mammal by modulating the
     activity of SK (claimed). Diseases treated by regulating SK cellular
     activity include rheumatoid arthritis, asthma, atherosclerosis,
     inflammation, meningitis, multiple sclerosis and septic shock.
     Dwg.0/14
FS   CPI
FA   AB; DCN
MC   CPI: B04-E03E; B04-G03; B04-G21; B04-G22; B04-L04; B11-C08E; B12-K04A;
          B14-A01; B14-C03; B14-C06; B14-C09B; B14-F07; B14-G02; B14-K01A;
          B14-S01; B14-S03; D05-H09; D05-H11A; D05-H11B; D05-H12A


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